

SYSTEM:OS - DIALOG OneSearch

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| Set | Items | Description |
|-----|---------|--|
| S1 | 20626 | KNOWLEDGE(W)BASE OR EXPERT(2W)SYSTEM# |
| S2 | 20977 | KNOWLEDGE(2W)BASE OR EXPERT(2W)SYSTEM# |
| S3 | 42399 | KNOWLEDGE(2W)BASE OR EXPERT(2W)SYSTEM? ? |
| S4 | 7386969 | DRUG? OR TREATMENT? OR MEDICINE? OR PRESCRIPTION? OR PHARM- ACEUTICAL? OR PILL? |
| S5 | 4219866 | DISEASE? OR MEDICAL(2W)CONDITION? |
| S6 | 7400130 | S4 OR REGIMEN |
| S7 | 1442 | S1(S)S6 |
| S8 | 252 | S7(S)S5 |
| S9 | 10 | S8 AND (DRUG(2W)(INTERACTION OR REACTION OR COMPLICATION OR CONFLICT)) |
| S10 | 252 | S7(S)S5 |
| S11 | 196 | RD (unique items) |
| ? | | |

DIALOG SEARCH 9/23/99

11/9/15 (Item 10 from file: 148)
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09355604 SUPPLIER NUMBER: 19212526 (THIS IS THE FULL TEXT)
UCSF Launches Website "HIV InSite," A Comprehensive Online Gateway to AIDS Knowledge.

Business Wire, p3170259

March 17, 1997

LANGUAGE: English RECORD TYPE: Fulltext

WORD COUNT: 1382 LINE COUNT: 00118

TEXT:

SAN FRANCISCO--(BW HealthWire)--March 17, 1997--UC San Francisco AIDS specialists announced today (March 17) that anyone with access to a computer and to the "world wide web" can now obtain the most comprehensive, credible and trustworthy HIV/AIDS information available online with just a click of the mouse.

The top-rated UCSF AIDS Program at San Francisco General Hospital and the UCSF Center for AIDS Prevention Studies (CAPS), programs of the UCSF AIDS Research Institute, have created "HIV InSite" -- a one-stop shop for reliable, peer-reviewed AIDS information and the only website in existence that contains research written, edited and maintained by frontline AIDS researchers from a health sciences institution.

The address for the site is <http://hivinsite.ucsf.edu>.

"Reliable, timely information is essential to developing effective responses to the HIV epidemic," said Paul Volberding, MD, UCSF professor of medicine and director of the UCSF AIDS Program at SFGH. "The internet offers the potential to arm decision makers throughout the world with accurate up-to-date information, fostering the development of sound policies, enhancing prevention program development, and providing people living with HIV with information about treatments that may extend their lives."

Unfortunately, AIDS information reported in the popular media is often incomplete or inaccurate, and those most in need of information may sometimes become overwhelmed or lost in cyberspace, according to Thomas Coates, PhD, director of CAPS and the UCSF AIDS Research Institute.

"Information found at HIV InSite is reviewed and presented by the top thinkers in the AIDS field," said Coates. "No other institution can offer such depth in this area."

"With the launch of HIV InSite, patients, physicians, researchers, policymakers, health service providers, community organizers and journalists can be ensured that they are accessing the most reliable and current online resource for AIDS knowledge," Coates added.

Surfers of internet and users of "HIV InSite" will benefit from the breadth of in-depth information on the site -- from treatment, clinical drug trials, epidemiology and basic research to social and policy issues, prevention programs, population subgroups, and ethics. A distinct advantage of HIV InSite is the ability of the user to "see the big picture" of the AIDS topic he or she is researching, thereby adding value to the search, said Nicole Mandel, project manager of the web site.

For example, a reporter in New Mexico who might be writing a story about HIV infection among teenage runaways may dialup the internet to find out prevalence statistics. Accessing HIV InSite, the reporter will not only find out HIV rates among this group, which can be broken down by regions or states, but will find facts on homelessness and AIDS, a research study on HIV prevention for high-risk youth, and lists of local and national advocacy groups working with young people.

Another scenario might include an outreach worker at a community-based organization in North Dakota who is working with prisoners for the first time. Visiting HIV InSite, he or she will find a list of prison-based HIV prevention projects, an evaluation of a post-incarceration followup programs at San Quentin, and a review of prison condom distribution programs.

"The comprehensive nature of HIV InSite adds value to the researchers' information search," Mandel said.

Pages or subcategories of HIV InSite include:

Medical

This area provides comprehensive, practical and state-of-the-art information to meet the needs of health care providers, clinical researchers, health care policymakers and those living with HIV disease. Highlights include a "trials search" -- a user-friendly database of all HIV clinical trials in the U.S. in which users may search by medical condition, drug or treatment name, or location to find locations of appropriate clinical trials. Another feature is the AIDS Knowledge Base -- considered by many researchers to be the "bible" of HIV disease -- a 1600-page online textbook that is edited by AIDS specialists from UCSF and SFGH. In addition, users may explore case studies, treatment guidelines, and clinical fact sheets.

Prevention

The goal of this section is to help service providers, researchers, educators and others build stronger programs and studies in the effort to prevent HIV infections. HIV InSite offers detailed resources to answer some of the most pressing needs in prevention, including pages on epidemiology, prevention basics, frequently asked questions and their answers, resources and links to basic information about HIV/AIDS and safer sex, and HIV prevention interventions that have been evaluated for effectiveness and have been published in scientific journals and government reports.

Social Issues

This section is a searchable, comprehensive index of HIV social and ethical issues, resources and analysis. The site contains policy resource materials, such as statements, guidelines, reports and analysis, and new developments on topics ranging from adolescents to workplace issues. The section catalogues and organizes policy information and resources from numerous sources, including federal, state and local legislatures and agencies, the courts, professional associations, health policy research organizations, AIDS community-based organizations and advocacy groups.

U.S. Map

A map of the United States includes state-by-state statistics of the epidemic, as well as links to AIDS agencies and resources available in individual states. The AIDS epidemic in the U.S. varies by metropolitan area and state, and accounts for a total of 7% of all cases of HIV infection in the world.

HIV InSite will expand this geographic guide to HIV to include other areas around the globe, but in the meantime has links to other HIV InSite pages or other websites that have international data. HIV-infected individuals will also be able to locate clinical drug trials in their geographic area by keying in their medical information either through the U.S. map or through the clinical section of HIV InSite.

Key Topics

This section includes comprehensive information on key HIV and AIDS topic areas. Users may look here for news, articles, opinion pieces, documents, abstracts, bibliographies, contacts and other information. Among topics included in the exhaustive list are: advances in treatment, African Americans, condoms, discrimination, health care workers, international, lesbians, Native American, needle exchange, Ryan White Care Act, schools, sex workers, tuberculosis, vaccines and women.

The UCSF AIDS Program at San Francisco General Hospital, founded in 1983, is one of the oldest and largest programs of its kind in the world. With an internationally-renowned faculty and extensive clinical and research activities, the AIDS program is on the frontline of advances in clinical care for people with HIV. The program received the number one ranking from U.S. News and World Report in 1996 for the sixth year in a row.

CAPS, established in 1986, is the largest consolidated research effort in the country focusing on the social and behavioral aspects of AIDS prevention and early intervention. Research activities are carried out locally, nationally and internationally.

CAPS also conducts ethical studies and policy analyses of AIDS-related issues, provides a program of technology transfer and exchange with community-based organizations, and trains U.S. and international scientists in AIDS prevention. CAPS is made possible through grant funding from the Office of AIDS and the National Institute of Mental Health.

HIV InSite is made possible by a grant from the Henry J. Kaiser Family Foundation, an independent health care philanthropy based in Menlo Park, California. The Foundation is not associated with Kaiser Permanente

11/9/32 (Item 27 from file: 148)
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05566716 SUPPLIER NUMBER: 11668048 (THIS IS THE FULL TEXT)
Computer-based knowledge systems.
Wyatt, Jeremy
Lancet, v338, n8780, p1431(6)
Dec 7, 1991
ISSN: 0099-5355 LANGUAGE: ENGLISH RECORD TYPE: FULLTEXT; ABSTRACT
WORD COUNT: 5478 LINE COUNT: 00443

ABSTRACT: In the first part of a two-part article, the author discussed the problem faced by physicians and other health care workers trying to keep up with the explosion of new medical information. In this, the second part, he discusses in detail the contribution that computers are making to the management and dissemination of medical information. Medical knowledge stored in computers may be used in four ways, but the author indicates that these four ways are interrelated and tend to overlap. One application of computer medical knowledge is hypertext. In this system, the reader is not limited to reviewing text and illustrations in a particular order, but can jump from tidbit to tidbit in any order which suits his need. A drawback of such systems is that the freedom of movement within a body of medical knowledge may result in the reader becoming lost or perhaps not appreciating the relationships between concepts which would be presented sequentially in a bound volume. A second, and very important, application of computer technology to medical knowledge is simply the maintenance of large knowledge files. Though such files might be called "databases", they are in fact knowledge bases and are more akin to reference books than to databases. A third contribution of computer technology to medical knowledge is specialized teaching aids. These systems are designed not for the professional seeking to add to his knowledge or perhaps look up a fact of which he is not certain, but rather for people to learn new things. The computer provides a presentation which may be individually tailored to the needs and abilities of the learner. The last category of computer applications to medical knowledge are the decision aids. These systems, somewhat akin to expert systems, help the physician by presenting the step-by-step sequences of decisions which must be made in the proper diagnosis of some symptoms or in the management of continuing treatment of patients. (Consumer Summary produced by Reliance Medical Information, Inc.)

TEXT:

In the first article I discussed medical knowledge and decision-making, the sources that doctors currently use to find this knowledge, and some of the drawbacks of these sources. I also described computer-based methods for searching bibliographic files. In this paper I concentrate on novel computer systems in which medical knowledge is not only stored and manipulated as text meaningful to human beings but is also encoded as symbols meaningful to computers.

There are four reasons to encode the knowledge held in a computer system:

- * To allow a computer user to move freely between passages of text, illustrations, or even sound recordings in a non-linear "hypertext" document.

- * To help a computer user find specific details in a large mass of medical facts stored in a "knowledge base", the electronic equivalent of a reference book.

- * To allow the computer to teach the user, by itself finding relevant details in its knowledge base that the user does not know (a teaching aid).

- * To allow the computer to help the user solve clinical problems, by itself finding details in the knowledge base that are relevant to the patient (a medical decision aid).

The key properties of hypertext, knowledge bases, and teaching and decision aids are listed in the table. These four kinds of system tend to overlap: in general, the more helpful a system is in decision-making about individual patients, the narrower its coverage of medicine (fig 1). For simplicity, I shall look at each kind in isolation.

Hypertext and hypermedia

When we use a textbook, we do not usually start at the beginning and read on to the end. Instead, we turn to figures or references on other pages, refer back to explanations in preceding chapters, and use glossaries and appendices to enhance our understanding. When text is stored on computer in the conventional way we are denied this instant access that the paper version gives us. However, these links can be recovered, and even enhanced, by the use of hypertext techniques [1] where links or short-cuts are provided between parts of the text. For example, a "definition" link may connect a word in the text with its glossary entry, while "see also" links draw attention to related sections of text. Frequently these links are shown as "buttons" or bold text on the computer screen, and users navigate through the system by selecting these items with a pointing device (mouse). Development of these systems can be difficult, especially if there is more than one author, since one has to keep track of multiple passages of text and their links as the work goes through successive revisions. Hypertext systems are now widely available outside medicine, guiding the uninitiated through software packages and tourists through airports. The Gosta's book project [2] is a medical hypertext system with 3000 links to help primary care physicians browse through the clinical and laboratory features of diseases.

Hypertext alone is no substitute for books in which diagrams or photographs are important. Thus, developers are now incorporating high-resolution computer graphics, sound, and video pictures to produce "hypermedia" systems. These are most widely used in teaching, and I shall discuss them in the section on teaching aids.

The similarity of one "page" to another in computer systems, the lack of a real beginning and end, and the fact that some hypertext systems offer ten or more links per page can lead to users getting "lost in hyperspace". To present a coherent overview and to avoid disorientation, some hypertext systems include a "guided tour" or maintain a list of all pages the user has viewed. Other systems provide an "overview" showing the structure of the whole document. [3]

Medical knowledge bases

Databases, the computer equivalent of card indexes, provide an efficient means for storing and retrieving large amounts of well structured data. If the store contains medical information such as drug dosages or **disease** incidences rather than patient data, the term "**medical knowledge base**" is preferred to database. There is a risk of overlap in terminology here, since **disease** incidences are calculated from a patient database, but few systems hold both kinds of information. Most knowledge bases include a search program to enable clinicians with modest computer experience to identify valid search items from lists and to combine them logically to identify relevant material. Medical knowledge bases can be stored on a central computer, with remote access by telephone or network links, or can be duplicated on floppy disk or compact disk read-only memory (CD-ROM) and installed on personal computers.

[TABULAR DATA OMITTED]

The difficulties of establishing and maintaining medical knowledge bases are identical to those associated with paper-based knowledge collections, discussed earlier. They include the difficulty of ensuring that the details contained are current and correct, that the coverage is adequate for clinical use, and that the index uses clinically relevant terms. However, two problems that are specific to electronic media are the use of symbols rather than a subtle natural language and the need to express knowledge in a form that can be read by any program running on any computer.

The London Dysmorphology Database is an example of a medical knowledge base distributed on floppy disk. [4] This details the mode of inheritance and clinical signs of 2000 congenital malformation syndromes. An editorial panel regularly reviews 1000 journals and issues annual updates. If congenital malformation interest you, it is difficult to see how this system can be bettered.

Floppy disks are not the ideal vehicle for knowledge bases because they are fragile and have limited capacity. A reasonable limit is 6, which will contain roughly 9 million characters equivalent to 1500 text pages. Instead, CD-ROMs are now widely used. These contain up to 660 million characters (the equivalent of 30 complete copies of the Oxford Textbook of Medicine), cannot be altered, and are physically more robust than floppy

disks. One of the knowledge bases available on CD-ROM (medical librarians usually keep a catalogue) is OncoDisk: this includes an oncology textbook, the Physicians' Data Query, and a catalogue of cancer therapy protocols known to the US National Cancer Institute, with details of patient selection, monitoring, and treatment, and even the names of physicians using the protocol. Some physicians already carry a selection of such knowledge bases with a portable CD-ROM reader and a notebook computer, to help them answer questions about patient management.

To keep a knowledge base current, updates must be sent out--a major enterprise if more than three or four a year are needed or the number of users is large. One solution is to allow access to a copy held and updated at a central point. An example is the Edinburgh Poisons Information System, which holds chemical and clinical data on thousands of poisons. [5] Access is gained through a Prestel terminal connected to a telephone line, and the system currently handles over 40 000 inquiries a year. Disadvantages of such dial-up knowledge bases are the need for special, sometimes arcane, search languages, and the slowness and cost of telephone links.

To allow wider access to centrally held knowledge bases, there are proposals by the European Community and others for "open systems interconnection". Establishment of an electronic "global village" will require standardisation of the codes used for clinical terms: but linkage of heterogeneous medical nomenclatures such as the ICD-10, SNOMED, and Read clinical coding systems, even through the "Unified Medical Language System", [6] has yet to be achieved. The physical linking of computer systems is easier, with fast cable, fibreoptic, or cellular phone links (which allow portable computers to communicate with their base [7]).

Teaching aids

Teaching aids likewise include a medical knowledge base and programs to frame and execute searches. However, they are designed to enhance knowledge and understanding by presenting facts, explanations, and examples at the user's own level, thus superseding the old "teaching machines" that subjected all students to the same material. The knowledge base might consist of facts about a disease, or differential equations linking physiological variables, together with a search program. These are coupled with a program that elicits and records the facts a student does not know by asking suitable questions. The search program then assembles the unknown facts, together with suitable text, to display remedial material, before retesting the student. More elaborate systems provide a glossary of terms and offer static or video images and feedback through voice synthesisers; many use hypertext techniques.

A slightly different approach is to use high-fidelity patient simulations, as in the "Mac" series. [8] 'MacMan', for example, consists of linked mathematical models describing the circulatory, respiratory, and fluid-balance systems with programs that allow the student to change key parameters and assess their effects on the simulated person; the mathematics are hidden behind an attractive graphic presentation which helps students to link their knowledge of anatomy and physiology and to learn about dynamic relations between body systems. [9] Students seem to like these commercial teaching programs. [10]

One reason why the early teaching machines were badly received is that isolated or gratuitously offered facts are not well remembered: students learn best when they are confronted with a problem, [11] especially if they are emotionally involved in its solution. Some of the technologies outlined earlier make it easier to simulate cases in realistic fashion. For example, it is now possible to include short sections of video showing a "patient" in a hospital setting with authentic background noises punctuated by a nurse requesting advice, and then give the user guidance according to his or her responses to an on-screen question. One annoying aspect of these systems is that a typing error or the wrong vocabulary can be misconstrued as ignorance. Research is now focusing on more "intelligent" tutoring systems.

The big drawback of all these teaching systems is the vast amount of work needed to assemble even a brief lesson, since there must be enough material to allow for all possible responses to each question. If the medium is interactive video, this means dozens, sometimes hundreds, of video clips, all of which must be filmed in the same location with the same actors. Consortia of medical schools and others are forming to build such programs, but new dilemmas have arisen such as the need for standards to

allow interchange of material, and the question of who owns copyright.

Medical decision aids

A medical decision aid has a **knowledge base** and search program similar to that of a teaching system, but contains a program that builds a patient model rather than a student model. At its simplest, this program may ask the user to type in responses to questions about a patient such as age, height, weight, and lung function results, and then formulates a suitable search of its **knowledge base**. In this example, the **knowledge base** contains formulae to predict normal lung function test results and information about what abnormal results mean. [12] Instead of symbols representing medical details or strategy articulated by expert clinicians, the **knowledge base** of some systems contains a mathematical distillation of a series of cases with known outcomes, such as the prior probabilities of **diseases** and the conditional probabilities of certain findings in patients with those **diseases**. [13] The programs that build the patient model and search the **knowledge base** comprise a "reasoner", which reconciles the clinical features of a patient logically or mathematically with the knowledge in the system, to produce inferences. Such inferences might include a list of possible diagnoses with their probabilities, [14] potential adverse **drug** reactions, [15] or the therapy recommended by an oncology protocol. [13]

The first computerised medical decision aid was built in the late 1950s, [16] and thousands have been made since then. They are best classified by their clinical role. One type interprets patient data--sounding an alarm, reporting on an ECG, [17] or highlighting abnormal laboratory test results. [12] The second kind requests the user to enter patient data, and proposes a differential diagnosis [18] or management plan. Decision aids of this sort are the commonest today, but they resemble a Greek oracle in their reluctance to allow their knowledge to be used for other purposes. [19] The third type allows a more flexible interaction, with more sophisticated search and model-building programs, so that user and system can negotiate jointly for solutions. [20,21]

Most medical decision aids use one of three reasoning methods--Bayes' theorem, decision theory, or symbolic reasoning or "artificial intelligence" techniques. Bayes' theorem tells us how to use probabilities derived from a database of past cases with a known outcome to calculate the probability of the outcome in an individual case. [14] Decision theory is an extension to Bayes' theorem that lets us add weightings representing the value of each possible outcome to a decision tree, to calculate the "expected utility". [22] Symbolic reasoning methods include the use of "if . . . then" rules and other complex computer models [23] to link clinical findings with their causes and management. All these reasoning methods have been refined since their introduction and are now being combined--for example, in directed acyclic graphs, [24] one of which [25] is shown in fig. 2. Other reasoning methods include obscure computational models inspired by the structure of brain. [26] These "neural nets" rely on a process called machine-learning, and their evaluation is far from easy. [27]

The patient simulators used by students can also be helpful to clinicians. For example, a program that predicts blood glucose profile over 24 hours with a specific insulin regimen [28] may allow a doctor to explore alternative managements for a patient in a series of computerised experiments that hold no risk for the patient.

Few of the developers of medical decision aids see them as anything other than animated reference books, complementing rather than replacing human knowledge. Not so Weed with his "Problem-Knowledge Coupler". [29] A coupler is a computer program designed to provide clinicians with all the medical details they need to tackle a specific clinical problem, without committing medical facts to memory. Couplers are available for some 15 common conditions at present: if widely adopted, such systems might have a revolutionary impact on medical education, but would leave their authors in a position of unique responsibility.

Medical decision aids have already proved themselves clinically, with the Leeds Abdominal Pain System halving perforated-appendix rates in a multi-centre study, [30] Pozen's chest pain system leading to a reduction in inappropriate admissions to a coronary care unit, [31] and ONCOCIN (a symbolic reasoner for assisting in protocol-driven care) improving the completeness of data collection in cancer patients. [32] Systems are being

built to address a clinical need, [33] but may raise complex medicolegal questions for their users and those who supply them. [34] However, there are also more immediate dilemmas for users and developers.

Limited scope of decision aids

No medical decision aid contains as much knowledge as a medical textbooks, and the intellectual and practical challenges of building and maintaining large knowledge bases to support doctors remain daunting. Although it is possible to express lower-level medical details in knowledge bases, making higher-level knowledge explicit is a complex "knowledge engineering" task that requires understanding about how to acquire, represent, and reason with knowledge. [23] There are similar problems with building large databases of patient cases and extracting summary measures from them to reason about new patients, who may not be drawn from a similar population. [35]

Some decision aids, however, have achieved good coverage of medicine. The INTERNIST system performed acceptably in diagnosis of a range of clinico-pathological cases from the New England Journal of Medicine. [18] It is now commercially available as 'QMR' on personal computers, covering over 600 diseases and 4300 patient findings. DXPlain is another broad-ranging system that was widely available through a computer network. [36] In Britain, the 'Oxford System of Medicine' is planned as a comprehensive flexible information system for general practitioners, and a prototype containing a fraction of the required knowledge has demonstrated that the project is technically feasible. [21] One alternative to building a single large **knowledge base** and then adding a reasoner is to integrate several different decision aids, perhaps even using different reasoning methods, into one flexible resource, such as the EXPLORER system built at Harvard. [3]

Difficulties of communicating with computers

Many people become frustrated when trying to persuade computers to do what is wanted. When a doctor feeds patient data into a decision aid, a good system will not only communicate its advice back but also convince the user that the advice is well based. With the 'QMR' system it took an experienced user between one and four hours to enter enough patient data to generate a useful differential diagnosis. [37]

Most decision aids communicate only by text. 'IntelliPath', however, includes a laser videodisk storing 5000 photomicrographs. [38] These are used to augment text definitions of histological features and to show which features best distinguish between possible diagnoses. Some 300 copies of the system, which is supported by the American Society of Clinical Pathology, have been distributed. Other methods that may assist in rapid and accurate data entry include graphic "user interfaces" (fig 3), handwriting and speech recognition, [39] and direct interviewing of the patient by computer. [14] The ideal, however, is to integrate decision aids with an electronic medical record, so that all relevant data are then available, as with the HELP system. [40]

How do decision aids explain their advice to the physician? One system allocates "weights of evidence" to each clinical finding; [14] others use their symbolic knowledge about anatomy, pathophysiology, or mechanisms of drug action to generate textual explanations of their reasoning; [23] yet others are able to explain not only how they arrived at their advice, but also how it would have differed had certain patient features been absent, or why an alternative explanation is implausible. However, as with intelligent tutoring systems, it is often difficult for the system to understand what kind of explanation is required.

Need for evaluation

A major concern is that computers, like doctors, are often unable to admit their ignorance. They also have enormous placebo power, exacerbated by the term "expert system", which may cause inexperienced doctors to accept their advice without question. Before any system is used to support patient care, we must be confident that it is giving sensible advice. The content of a decision aid's knowledge base, the rigour of its reasoning, and its performance on suitable test cases must all be examined. [41] Even if the decision aid's performance is promising, it may still lack beneficial impact if it is difficult to use or gives implausible advice: [42] as with drugs, controlled clinical trials are the only way to assess their impact on doctors and patients. [41]

An ideal knowledge system

What every doctor needs is a portable, accurate, and adaptable source of medical knowledge. At present, nothing of the kind exists; but it is not too soon to think about the features required of such a system. What follows is based partly on the surveys of doctors discussed in the first paper. [43-45]

The system must be comprehensive

The system should cover the majority of diseases, therapies, and investigations as well as basic medical sciences, and should integrate text, graphics, moving images, and sound.

Knowledge contained in the system must be current, accurate, and verifiable

The certainty of the details stored should be stated, together with their sources to allow easy verification. The system should maintain its own record of the age of its knowledge, and updates should be issued regularly; all information should be safeguarded against unauthorised modification. To avoid ambiguity and to ease maintenance, a consistent vocabulary should be used, possibly even a logical language. [21]

Knowledge in the system must be easily accessible, where doctors see patients

The system should be portable and unobtrusive--preferably fitting into a white-coat pocket--and also cheap, indestructible, and workable without special equipment. To assist in clinical decision making, it must be fast and easy to use. Instead of a typewriter keyboard which is bulky and slow, the system should incorporate hand-writing recognition (like the new generation of pen-input computers). [46] The indexing system should include abbreviations and synonyms used in clinical practice; cross references to MeSH would facilitate literature searches. To help users absorb new material, updates should include digestible text overviews, analogous to the reviews and editorials in the medical weeklies.

The system should be adaptable

Since clinicians will be using the system throughout their working day, it should accommodate electronic notes and be adaptable to their own preferred terms or abbreviations. This could be achieved if each doctor carried a personal electronic badge which broadcast their identity and other data to the system in their hands. [7] The system should also be able to adapt itself to specific clinical problems, tailoring its reports and advice according to patient features. To do this, it could be linked by cellular radio networks to clinical data systems. This would also help it to predict, from information on who was using it and where, what knowledge the physician might need next--"anticipatory computing". [47]

Conclusions

There are few systems that meet even one of the above criteria, but advances in information technology will make the ideal knowledge system technically feasible. Furthermore, developments in medicine itself, and in the administrative framework surrounding it, suggest that the intellectual and practical challenges will be met.

One development is that medical societies are taking increasing responsibility for their members' knowledge as well as their professional competence. [48] Thus, specialty societies are defining management protocols, minimum data sets, and the content of coding systems. However, establishing and maintaining a fund of medical knowledge is a major undertaking, and few specialty bodies will have the resources to do it.

Another development is the establishment of medical informatics as the discipline concerned specifically with the acquisition, storage, and communication of medical knowledge and data. [49,50] Training courses, academic departments, professional journals, and societies now exist, [51] together with a definitive textbook. [52] The big issues in medical informatics include how to represent and store medical knowledge electronically and how to help doctors extract knowledge from these stores and apply it to their patients. Collaboration with specialists in medical education, computer science, and medical cognitive science [53] will be necessary to resolve some of these questions. A further challenge is to find ways of evaluating and comparing the sources of knowledge, and of assessing their impact on medical decisions (and on patients).

If the medical profession could harness the medical, technical, and managerial skills and produce a system such as that described above, the quality of medical care could take a quantum leap forward. Some clinicians may argue that reliance on such support will degrade their skills. This was

the cry when Laennec introduced the stethoscope.

These two papers were written partly at the National Heart & Lung Institute, London, and partly while I held an MRC travelling fellowship at the Section on Medical Informatics, Stanford University. I gratefully acknowledge the assistance of colleagues at both sites, others who have contributed their time, and the staff of the Lister Hill National Center for Biomedical Communications, US National Library of Medicine.

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CAPTIONS: Characteristics of computer-based knowledge system. (table); The continuum of medical knowledge systems. (graph); The directed acyclic graph underlying the ALARM anesthesia monitoring system (chart); Sample screen from ONCOCIN system. (diagram)

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DXplain; An Evolving Diagnostic Decision-Support System (SPECIAL COMMUNICATIONS)

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ABSTRACT: DXplain is an evolving computer-based diagnostic decision-support system designed for use by the physician who has no computer expertise. DXplain accepts a list of clinical manifestations and then proposes diagnostic hypotheses. The program explains and justifies its interpretations and provides access to a knowledge base concerning the differential diagnosis of the signs and symptoms. DXplain was developed with the support and cooperation of the American Medical Association. The system is distributed to the medical community through AMA/NET -- a nationwide computer communications network sponsored by the American Medical Association -- and through the Massachusetts General Hospital Continuing Education Network. A key element in the distribution of DXplain is the planned collaboration with its physician-users whose comments, criticisms, and suggestions will play an important role in modifying and enhancing the knowledge base.

SHORTLIFFE (Ref. 1) defines a computer-based medical decision-support system as a computer program designed to help health professionals make clinical decisions. Under this broad definition, there are many decision-support systems in use today. They include such applications as clinical laboratory systems, pharmacy systems, and radiology reporting systems. For the most part, these are "passive" information management tools. That is, they make information more readily available to the physician but they do not provide "active" decision support by applying medical knowledge to a specific patient's data, nor do they recommend a specific conclusion or course of action.

There has been less success in developing active systems. One strategy used in such systems applies predefined rules to the patient's data and alerts providers to conditions that might require action. The most successful system for inpatient care is the HELP system. (Ref. 2) In ambulatory medicine, two examples of systems that provide patient-specific recommendations for ambulatory care are CARE (Ref. 3) and COSTAR. (Ref. 4) There are also a few examples of "expert" systems that guide the physician in treating certain complex, but well-defined, conditions; eg, the ONCOCIN system. (Ref. 5) These systems contain in-depth knowledge about a well-defined subset of medical knowledge and require considerable and detailed information about the patient's clinical status to provide the computer-generated consultations.

Computer-aided diagnosis in general medicine requires a much broader level of decision support. There have been a number of provocative research efforts in computer-aided diagnosis, (Ref. 6-9) but these have been research prototypes whose contributions were primarily methodological. With the exception of the work by deDombal et al, (Ref. 10) these programs were not made available to the practicing physician. There are a number of reasons to explain the limited impact of information technology in the diagnostic aspects of medical decision making. (Ref. 1,11,12) Major

problems have included difficulty in accessing and interacting with the systems, a limited area of application (eg, one of the most successful computer-aided diagnosis programs is limited to the differential diagnosis of the acute abdomen (Ref. 10)), a limited ability of the systems to explain and justify the interpretations, and less than acceptable quality of the interpretations. Some investigators believe that there are major intellectual and technical problems that must be solved before there can be a truly reliable consulting program. In particular, it is claimed that computer programs must be able to incorporate pathophysiological knowledge and causal relationship based on pathophysiological reasoning. (Ref. 12)

We accept the validity of these concerns, but take a more optimistic position concerning the potential for using currently available knowledge and technology to assist the physician in the information needs of daily practice. A recent study suggests that the information needs of physicians in office practice are not being met by printed sources such as textbooks and journal articles. (Ref. 13) Of the practice-related questions that were identified, 25% involved the diagnosis of symptoms, physical findings, or syndromes. We believe that a significant portion of the practical needs of clinical medicine can be met now by providing ready access to a computer-stored knowledge base of diagnoses and their associated signs and symptoms.

We believe it is possible to develop a computer program that uses an extensive knowledge base and relatively simple computational models to provide significant diagnostic problem-solving assistance to the practicing physician. The program should allow the computer-naive user to enter a set of signs and symptoms using a typical medical vocabulary. The program would then generate a list of hypotheses that deserve consideration, comment on the diagnostic relevance of each sign and symptom, and suggest specific additional data elements that might clarify the differential diagnosis currently favored by the computer model. (Ref. 9,14-16)

This article describes DXplain, an evolving computer-based diagnostic decision-support system designed for use by the physician who has no computer expertise. (Ref. 14) DXplain accepts a list of clinical manifestations and then proposes diagnostic hypotheses. DXplain explains and justifies its interpretations and provides easy access to a comprehensive knowledge base concerning the differential diagnosis of the set of signs and symptoms.

DXplain does not attempt to make a single diagnosis to mimic the behavior or replace the judgment of the expert clinician. DXplain has a less ambitious, but perhaps more attainable goal: to suggest a list of diagnoses that should be considered given a particular set of signs and symptoms. Because DXplain is in a continuing state of development, we have labeled it an evolving diagnostic decision-support system. Our plan is that DXplain will continue to improve through collaboration with its physician-users whose comments, criticisms, and suggestions will play an important role in modifying and enhancing the knowledge base and the algorithms used in the computer-generated interpretations.

SYSTEM CAPABILITIES

We believe that the following six criteria are important for a differential diagnosis decision-support system intended for use in routine clinical practice. The system should (1) be easy to use by physicians who have little or no computer background; (2) be based on comprehensive medical content; (3) provide correct and accurate interpretations; (4) justify its interpretations; (5) be convenient to access from the physician's office, hospital, or home; and (6) evolve and improve as a result of user criticism and analysis of user sessions.

Easy to Use

It has been the general experience that few practicing physicians will use computer programs requiring extensive training or knowledge of computer technology. DXplain demands little knowledge of computer technology and requires only the use of the vocabulary common in medical practice. On-line help is available for an explanation of the system commands.

As with any decision-support system, DXplain uses a controlled vocabulary for communicating patient information to the system. Computer technology has not yet progressed to the stage in which a computer program can recognize the free-form narrative text that a physician might use to

describe clinical manifestations in a medical record or with a colleague. The predefined medical vocabulary used by DXplain consists of more than 4700 terms based on the clinical and basic laboratory data that might be collected in an ambulatory practice or in the emergency department.

DXplain has several features that assist the user in selecting the desired terms from the controlled vocabulary. For instance, there is extensive synonym and abbreviation terminology; also, the system can recognize and correct many misspellings. DXplain can recognize terms that are "close" (eg, "congestive heart failure" and "heart failure"), as well as synonyms for terms at both the single-word level (eg, "kidney" and "renal" are equivalent in many different terms) and at the fullphrase level (eg, "anisocoria" is equivalent to "pupillary inequality," "factor VIII deficiency" is considered equivalent to "hemophilia"; and "blood glucose elevated" is considered equivalent to "hyperglycemia"). In addition, many abbreviations are recognized (eg, "ESR" and "CHF") to speed data entry.

The DXplain vocabulary structure is hierarchical, which allows flexibility in specifying the precise level of detail of the clinical manifestation. Thus, DXplain groups more specific terms (such as "lower abdominal pain") under a less specific term (such as "abdominal pain"). This hierarchy is important for both the user interface and the algorithm used for interpretation. When a user enters a specific term, such as "right lower quadrant pain," all of the appropriate less-specific terms, such as "lower abdominal pain" and "abdominal pain," are assumed by the system, but related terms at the same level of specificity, such as "left lower quadrant pain," are not assumed.

A typical user interaction with DXplain is illustrated in Fig 1. Examples of how the system helps the user select the appropriate terms during input are illustrated in Fig 2.

A second important factor relating to ease of use is the rapidity with which the user can enter the clinical manifestations and extract the desired information and interpretation. The system is designed to be largely self-explanatory. There is no need to read manuals: the beginning user can take advantage of menu selection; the experienced user can make use of an abbreviated command language to speed the interaction. The requirement for rapid time response was a critical design factor that influenced decisions made about the organization of the knowledge base in the computer. It requires about two minutes to complete the dial-in sequence to log on to AMA/NET and to connect to the computer located at Massachusetts General Hospital. The entry of the seven terms illustrated in Fig 1 required about one minute. Evaluation of the clinical data by the computer program and presentation of the interpretation and list of diagnostic hypotheses takes from 10 to 20 s.

Accurate and Comprehensive Medical Content

The development of a comprehensive knowledge base in medicine, whether printed or computer based, is a large effort. The merit of any decision-support system depends to a significant extent on the quality of the knowledge base used in formulating its recommendations. One aspect of any knowledge base, whether printed or computer based, is the inability of the author to certify that the entire knowledge base is totally accurate and comprehensive.

There are no methods to extract automatically the relevant information from the published literature. In fact, the published literature is not as useful as desired since it often does not provide the quantitative relationships between clinical manifestations and diseases that are required for a decision-support system. For example, one frequently finds statements like "symptom X is 'occasionally found' in the disease" or "it is 'not uncommon' to have symptom Y" or "the 'great majority' of the patients with the disease will demonstrate symptom Z."

To provide the necessary knowledge base for DXplain, we begin with the computer-based version of Current Medical Information and Terminology (CMIT), which is published and supported by the American Medical Association. (Ref. 17) Current Medical Information and Terminology contains summaries of information concerning the etiology, signs and symptoms, laboratory findings, and disease course for more than 3000 distinct diseases, disorders, and conditions.

To transform this knowledge base into one suitable for a decision-support system, it was necessary to carry out a considerable

amount of manipulation and additional content acquisition. For the disease list for DXplain, we combined some diagnoses from CMIT to form more inclusive definitions, while others were subdivided into more specific forms of the disease (eg, separate stages of a disease, forms of the disease specific to certain demographic groups, and forms attributed to different etiologic agents). Additional diseases were added when deficiencies in CMIT were noted.

As the first step in specifying the controlled vocabulary of terms to represent the clinical features of each disease, terms were extracted from the text of CMIT, yielding a list of some 6000 words and phrases. An extensive review of this list was undertaken to lend coherence to the vocabulary. Synonyms were merged where appropriate and similar terms were linked together in a hierarchical manner to express their relationships (usually in terms of such qualifiers as severity, duration, or anatomic location). The outcome was a term directory consisting of 4000 descriptors. As disease descriptions were compiled, 700 additional concepts were added to the directory.

We used a three-step process to generate the disease-term relationships of the knowledge base. First, a list was compiled from the CMIT data base and from expert judgment of all the terms that had some role in either supporting or ruling out a particular disease. Next, medical texts were reviewed to determine the frequency of each clinical finding in the disease. Where necessary, in circumstances of recent discoveries or obscure conditions, literature searches were conducted to supplement standard references. Finally, an estimate of the potential for the presence or absence of each term to evoke or refute the diagnosis was made.

This content development was an iterative process that was done by the system developers in collaboration with 13 physicians representing several medical disciplines. Because of the number of individuals involved, extensive discussions were required to reach a consensus on content and assignment of appropriate weighting factors for the relationship of terms to diseases. Once guidelines were established, authors were trained in filling out work sheets for each disease. Each work sheet included all terms that had been previously assigned, a prescribed set of demographic terms (age, sex, and duration of symptoms), and a generous number of blank lines for adding new terms. After the work sheets were completed, one of us (J.J.C.) reviewed them to ensure consistency of content, terminology, and assignment of evoking potentials.

The result of this work is DXplain's knowledge base consisting of descriptions of approximately 2000 diseases, about 4700 terms (signs, symptoms, and more), and some 65 000 relationships among them. On average, each disease description contains relationships to 35 terms. Each relationship identifies the frequency of the manifestation among patients with the disease and the strength with which a manifestation evokes a diagnosis for consideration.

From a practical viewpoint, it is impossible to verify completely all the elements in a knowledge base that is the size and complexity of DXplain. We believe that there must be a continuing effort to detect and correct incomplete or inaccurate disease descriptions. In addition, the knowledge base can never be static, but must continue to evolve as new knowledge is gained and new evidence is identified about each disease.

One of the major advantages of having the knowledge base reside on a single central computer is that the knowledge base can be updated easily and as often as necessary. The addition of a new term, disease, or synonym, the modification of the descriptor-disease relationship, or the enhancement of the program can be done quickly. Because these changes are immediately available to all users, the system can be dynamically responsive to user suggestions concerning deficiencies and improvements.

Provide Correct and Accurate Interpretations

In designing a differential diagnosis decision-support system, we assumed that the most useful assistance that can be provided to the practicing physician is to suggested the reasonable diagnoses that should be considered, given any particular set of signs and symptoms. We believe that in many complex diagnostic problems (and many not so complex), a major reason for not making the correct diagnosis is the failure of the physician to generate a differential diagnosis list that is comprehensive enough to include the correct diagnosis, yet sufficiently focused to include only the

more likely diagnostic possibilities.

The goal in DXplain is to assist the physician in two phases of the process of differential diagnosis: (1) to remind the physician of diseases that should be considered as possible candidates to explain the patient's condition and (2) to provide information about specific diseases that might be eliminated from consideration. We explicitly reject the objective of determining the "correct" diagnosis. We reason that the clinician will always have a more complete picture of the patient than will be entered into the computer program and that a more realistic goal for a decision-support system is to bring to the user's attention the plausible explanations for a patient's signs and symptoms. The user may then consider which diseases are appropriate to the case by applying common sense, clinical experience, and full knowledge about the patient and, possibly, by further interacting with the program.

DXplain is not intended to aid the specialist working in his/her specialty area. Thus, the cardiologist dealing with a patient with a complex murmur is unlikely to find DXplain very helpful; but the cardiologist dealing with a patient with abdominal pain may obtain useful assistance. The most obvious way in which DXplain can help is in suggesting obscure or rare diseases that may be rarely seen by most physicians. DXplain also may be helpful by suggesting diseases that present in atypical ways.

DXplain uses a relatively straightforward algorithm to select its list of plausible diagnoses. This algorithm has been described in a previous publication. (Ref. 14) The DXplain selection rule takes advantage of conditional probabilities and a scoring system similar to a Bayesian computation. Models such as this have been frequently used in other diagnostic decision-support projects, the most influential being the ranking algorithm used in INTERNIST/QMR. (Ref. 7,14) Our development of DXplain was strongly influenced by the experiences and the limitations of the original efforts of Miller and colleagues with INTERNIST, and their later development of QMR.

The knowledge base for DXplain contains more than 65 000 relationships between diseases and patient descriptors (or clinical manifestations). The format for these relationships and the data structures are similar to the format and data structures used in the INTERNIST/QMR system (Ref. 7) except that in DXplain terms cannot only support a given diagnosis, but can also contradict other diagnoses. The relationships in DXplain are concerned with three different elements: (1) term importance, (2) term frequency, and (3) term-evoking power.

Term importance is used to express how significant the particular term is in indicating the presence of disease. A high term importance is given to findings that can be identified with high reliability or are rarely found in healthy persons and, therefore, should be explained by some disease within the differential diagnoses.

Term frequency is used to identify how often a particular term is expected to occur in a specific disease. The possible values for term frequency can be one of seven different states ranging from "always" to "never."

Term-evoking power is used to identify how strongly a particular term supports the possibility that a specific disease might be present. This term is related to the concept of predictive value positive (the predictive value of a positive test -- this is the probability of a disease being present given the presence of a certain finding). The possible values for term-evoking power can be one of eight different states ranging from "certainly supported" to "weakly supported" and from "weakly contradicted" to "strongly contradicted."

DXplain uses the numerical values of these different relationships to derive the list of the diagnoses that should be considered (Fig 1). DXplain selects diseases to be included on this list on the basis of how well the manifestations of a particular disease match the descriptors that have been entered by the user. The diseases are presented to the user in two lists: "common diseases" and "rare diseases"; in addition, a serious disease (one that may require relatively immediate action) is so indicated on the list by an asterisk.

The user can request DXplain to explain why any specific diagnosis was included (Fig 3). DXplain will present the clinical findings entered by the user that support the selection of that disease, the clinical findings that

would not be expected in that disease, and additional clinical findings that would be expected if that disease was present. In this way, DXplain assists the user in understanding the logic used by the program and facilitates pattern matching by the user in comparing DXplain's disease description with his/her knowledge about the patient. The intent is to present sufficient information so that the user can always use his/her own clinical judgment as to the appropriateness of DXplain's interpretation.

The user can ask DXplain to consider a specific diagnosis that was not included on the initial list (Fig 3). DXplain will then present the same analysis, as described in the previous paragraph, for the diagnosis under consideration and, furthermore, will include this diagnosis in any later interpretation after additional findings are entered.

The user can change DXplain into an interrogative mode wherein the system will question the user about the presence or absence of significant findings that have the potential for clarifying DXplain's current differential diagnoses (Fig 4). This mode is particularly useful in helping the user select the clinical manifestations that are important without forcing them to enter a large number of less relevant findings. At any time in this mode, the user can interrupt DXplain to ask "Why?" ie, to ask DXplain to justify why this particular clinical manifestation is important. DXplain will respond by displaying the name of the disease that is being considered at that point in the interaction and the reason the particular finding might be important in confirming the presence of that disease.

DXplain's ability to explain and justify are key elements of the system. It is critical that this system not be perceived as a magic black box that can somehow provide the "answer" to a complex diagnostic problem. We believe that physicians will not accept DXplain as a useful diagnostic assistant unless the clinical interpretations seem reasonable and unless the system can offer explanations that are understandable and persuasive. (Ref. 18)

Convenient to Access

Almost a decade ago, Shortliffe wrote: "A recurring observation as one reviews the literature of computer-based medical decision making is that essentially none of the systems has been effectively utilized outside of a research environment, even when its performance has been shown to be excellent." (Ref. 8) For the most part, this observation is still true today. One important barrier is that the practicing physician cannot easily access a computer-based decision-support system from his/her office, or any other location, at any time. There are a number of systems that are available in university hospitals and that are of great importance in the host institution and have considerable value as demonstration models. However, none of these systems provide support to the practicing physician on a national scale.

DXplain is unique in that the decision-support capability is easily accessible using only a simple computer terminal (a microcomputer can also be used to make the connection), a telephone modem, and a telephone call (usually a local number in most of the major cities of the United States). DXplain is also available in a similar fashion in Canada and Japan. There is no start-up cost associated with purchase of the programs or of the knowledge base. Many physicians already have the necessary technology to access DXplain since the needs are the same as those used for on-line bibliographic search services.

DXplain was developed with the support of the American Medical Association and is designed to be distributed to the medical community through AMA/NET -- a nationwide computer communications network sponsored by the American Medical Association. Physicians and other professionals can access the system through the AMA/NET. Medical schools and teaching hospitals can access the system either through AMA/NET or through the Massachusetts General Hospital Continuing Education Network. In both cases, the cost of accessing DXplain is directly dependent on the length of time one is connected to the system.

A subscriber to AMA/NET can also access information data bases (EMPIRES clinical reference citations, Medical Procedure Coding and Nomenclature, the Associated Press Medical News Service, and more), public information services (Centers for Disease Control Information Service, National Library of Medicine/National Institutes of Health Information Services, Adverse Drug Reaction Reporting Form, and more), electronic

mail, and the Massachusetts General Hospital interactive medical education courses (Hoffer et al (Ref. 19)). AMA/NET also provides documentation and telephone support to its subscribers. (For information on AMA/NET, call 1-800-426-2873; for information on the Massachusetts General Hospital Continuing Education Network, call 617-726-3950.)

Evolve and Improve as a Result of User Criticism

A key element in the distribution of DXplain is an integrated electronic mail capability. At any point in the interaction a user may enter a comment or question into the computer system. This electronic mail is read at frequent intervals by the system developers at Massachusetts General Hospital and responded to as appropriate.

We view the plan for the continuing improvement and enhancement of DXplain as one of the more important aspects of its development. The major potential weakness of any diagnostic decision-support system such as DXplain is the quality and completeness of the underlying knowledge base. Evaluating a clinical decision-support system is difficult, both conceptually and in practice. (Ref. 1,11) Systematic clinical trials or formal outcome studies on the impact either of computer-based knowledge bases or of medical textbooks are logistically almost impossible. DXplain has been used by physicians for over 500 hours at more than 40 different test sites in the United States, Canada, and Japan. The initial user acceptance and peer review has been favorable, although the evaluation has been largely anecdotal.

The continuing refinement of DXplain will be most fruitful if the planned collaboration between the physician-users and the developers materializes. We expect and need the participation of physicians who will challenge the system with rare diseases and with uncommon manifestations of common diseases. The continuing critical review by DXplain users of the knowledge base and interpretations of the system will provide important feedback in the iterative process of knowledge base development.

SYSTEM LIMITATIONS

DXplain has a **knowledge base** that covers more **diseases** than are discussed in most textbooks of **medicine**, but in some areas DXplain is incomplete, eg, there is only limited coverage of dermatologic **diseases**, where diagnosis often depends on the visual appearance of the lesion. At present, there is only minimal coverage of **diseases** from psychiatry and orthopedics. DXplain presently allows the entry of only a limited set of laboratory test findings. The original design goal of DXplain was primarily focused on ambulatory **medicine**; as a result, the current version of DXplain does not allow the entry of many of the complex laboratory tests that are performed only in hospitals. We are continuing to add both **diseases** and terms, including the most common laboratory abnormalities.

DXplain can cope in only a limited fashion with the variations in the way that a disease can present based on its evolution over time, degree of severity, and the modifications introduced by therapy. In addition, DXplain does not identify complex disease patterns caused by the presence of two or more diseases in the same patient. DXplain considers each disease and its expected manifestations as unique entities. DXplain is unable to recognize how the manifestations of one disease can be modified by the presence of a second interacting disease. However, DXplain will attempt to select and present to the user all the individual diseases that might account for the more important findings so that the physician can use clinical judgment to carry out any appropriate recognition of disease patterns.

A number of authors have emphasized the importance of an explanation capability to encourage physicians to use decision-support systems. (Ref. 1,18) DXplain has an explanatory capability, but it is limited to the justification of why a particular disease should be considered (or ruled out), based solely on the likelihood of occurrence of the specific clinical manifestations in that disease. DXplain has no pathophysiological or anatomic knowledge and no ability to consider pathophysiological or anatomic reasoning.

The mere existence of data in a knowledge bank is, of itself, no guarantee of completeness and accuracy. The same professional judgment and critical appraisal are required when using DXplain as required when reading a medical textbook or discussing a patient case. In fact, since the computer program does not possess the depth of medical knowledge, the

wisdom of medical experience, or the ability of a colleague to reason, it would be wise to be even more critical of the computer's interpretation. One of the weaknesses that is common to every computer-based decision-support system is a lack of "common sense" and a relative inability to consider important personal, social, family, and employment factors of the particular patient. This deficiency is well illustrated by an anecdote in the conclusion of Shortliffe's article. (Ref. 1)

We believe it is critical that the physician retain the ultimate responsibility for identifying the correct diagnosis or diagnoses in any given patient. Using DXplain should be considered similar to consulting a medical textbook or journal article. DXplain should be used only as an adjunct, an information base, and a well-specified medical knowledge resource; DXplain cannot be a replacement for the clinician's knowledge and experience.

CONCLUSIONS

The potential contributions of computer-based decision-support systems are based on several factors: (1) the increasing complexity and scope of the medical knowledge base, (2) the increasing fragmentation and specialization of medical practice, (3) the increasing availability and affordability of powerful computer technology, and (4) the increasing willingness among physicians to utilize computer technology in all phases of patient care activity.

DXplain is an evolving computer system that uses an extensive knowledge base and relatively simple computational models to provide significant diagnostic problem-solving assistance to the practicing physician. The program allows the computer-naïve user to enter a set of patient signs and symptoms and then generates a list of hypotheses that deserve consideration. The system also comments on the diagnostic relevance of each sign and symptom and suggests specific additional data elements that might clarify the differential diagnosis currently favored by the computer model. The advantages of a dynamic, interactive, evolving reference tool, such as DXplain, over static, passive textbooks and journal articles are exciting.

DXplain is unique in being a decision-support system that is easily and inexpensively available to a large number of physicians through nationwide medical information networks. A key element in the distribution of DXplain is the planned collaboration with its physician-users whose comments, criticisms, and suggestions will play an important role in modifying and enhancing the knowledge base and the algorithms used in the computer-generated interpretations.

The most important evaluation of DXplain will be made by the physicians themselves as they attempt to use the system in their daily practice. As DXplain is used in a variety of practices with a variety of information needs, we will learn whether this system is capable of providing clinicians with useful information in a timely manner. The measure of success is not whether the ultimate diagnosis is listed first or fourth in the DXplain list of plausible diagnoses, but whether the physician-users perceive that the use of the system has added to their understanding of the patient's problems. Through careful analysis of user interactions, comments, level of satisfaction, and system performance, we expect to learn much about DXplain's ability to provide assistance in making clinical decisions. Based on our experience during the testing phase, we are optimistic that DXplain will be a useful educational resource and an effective assistant to the physician in daily practice.

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Computer-assisted medical decision-making: interest growing (MEDICAL NEWS
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Computers can never replace physicians. Only physicians have the ability to reason logically and to mix that reason with intuition, experience, and ethics -- something no machine can ever learn to do."

Or so many physicians have been telling people proposing computer-assisted medical decision making (CMD) since the early 1960s, and controversy has continued. But now it looks like the two sides are nearing agreement: Computers may never replace physicians, but they can and will assist their decisions.

"Assist" is the key word in CMD. Early advocates tended to overestimate the powers of the computer and promised complete clinical evaluation at the push of a button. It was natural for physicians to feel somewhat threatened. It was also natural that, with experience, such promises had to be modified.

Today there still are only several functioning knowledge-based decision systems -- called "knowledge-based" because they make inferences using a data base of medical information stored in a computer's memory -- and they are extremely modest. More complex systems are currently under development, but even these will merely serve as expert consultants; the ultimate decision, which requires personal, occasionally subjective considerations, still will rest with the practitioner.

"The early systems attempted to do diagnosis for the doctors -- which is crazy," says Francis T. de Dombal, MB, MD, consultant with the Leeds Area Health Authority and Reader in Clinical Information Science at the University of Leeds, England. "Doctors do some things very well indeed, and computers do them very badly. For example, if the Leeds United Football Team was playing at home, there'd be quite a lot of people with bellyaches. The experienced doctor would know the source of all these bellyaches, and he wouldn't take everyone's appendix out. The computer might well do so."

de Dombal is well acquainted with the abilities and limitations of computers: His Leeds system was one of the first and remains one of the few fully operative CMD systems. Able to discriminate between common causes of acute abdominal pain, the system has been used for the past eight years in three United Kingdom (UK) hospitals, and recently the UK government authorized and funded a three-year trial in 11 other hospitals.

Although both the problem and the possible diagnoses are limited, the system has improved diagnostic accuracy for abdominal pain by 20%, according to de Dombal. After studying the pattern of admittances in his own hospital and others, he and his team constructed probabilities of common causes of abdominal pain and entered these into the computer memory along with the signs and symptoms associated with each cause.

'What Have I Got, Doc?'

When a patient is initially seen with abdominal pain, the examining physician records observations on a preprinted form that requests information about the pain, other symptoms, medical history, and findings from the general examination. The physician then gives the form to a member of the computing team, who enters it into the computer by choosing an "answer" for each of a series of categories. For example, under the category of "relieving factors," he can choose between "lying still," "vomiting," "antacids," "food," "other," and "nil." Other categories include sex, age, site of pain at onset, aggravating factors, and site of pain at present.

Next the computer analyzes the data. Essentially, it compares the

details of the new case with those of hundreds of similar cases in its memory and uses a theory of probabilities to calculate the likelihood of various diagnoses. The resulting printout displayed to the physician lists all the symptoms and gives the probabilities that the patient has appendicitis, non-specific abdominal pain, diverticular disease, perforated peptic ulcer, cholecystitis, small bowel obstruction, or pancreatitis. A sample printout might suggest a 27.11% chance of appendicitis, a 12.28% chance of perforated peptic ulcer, and a 60.60% chance of nonspecific abdominal pain; the practitioner can combine this information with his clinical impressions to arrive at a diagnosis.

"I would defend to the death the doctor's right to override what comes out of the computer if he thinks it's crazy," stresses de Dombal. "Right across the top of all our systems it says, 'Clinical judgment must take precedence; these are only suggestions.'"

After testing the system from January 1971 to August 1972, de Dombal found that preoperative diagnoses made with the computer-aided system (using data provided by the registrar) were 91% correct. This was in comparison with 42% correct for diagnoses made by unaided admitting physicians, 71% correct for diagnoses made by unaided house surgeons (less than six months experience), 79% correct diagnoses by unaided registrars (between one and two years surgical experience), and 81% correct diagnoses by unaided senior clinicians (more than five years surgical experience). These results show one obvious advantage of the system: training inexperienced physicians.

"What we're really trying to do," says de Dombal, "is to get the inexperienced doctor's level of performance up to that of the senior clinicians within a few weeks, as opposed to ten years."

The improvement figures may be misleading, however, since the physician often makes the crucial decision before turning to the computer.

"Before these trials were run," says Richard Bruce Friedman, MD, associate professor of medicine and human oncology at the University of Wisconsin Medical School, Madison, "the investigators had already screened out every area but abdominal pain. By the time (Ref. aphysicia) knows it's abdominal pain, he calls the surgeon and he gets an x-ray -- even without a computer. The test is an artificial situation and makes no real difference to clinical procedure."

"Even if you send this program neck pain, it will still make a diagnosis of abdominal pain."

It seems to make a difference to some physicians, though. With the help of the World Organization of Gastroenterology, investigators have modified the data base to take geographical variation into account, as abdominal pain may have different causes in different areas. And since 1972, the cost of the program has come down considerably: Once run on a large university computer, it now can run on small computers like Pets and Apples, which are quite common in hospitals and physicians' offices these days.

Moreover, the US Navy is currently evaluating de Dombal's program for use on submarines and is adapting the data base to this population. According to George Moeller, MD, director of the Behavioral Sciences Branch of the US Navy, appendicitis is one of the principal medical problems aboard submarines. Although some medical problems can be handled aboard, surgery of course requires moving the patient off the submarine.

"That's something we would like to avoid," says Moeller, "not only because it (Ref. movigthepatiet) would interrupt the mission but because it's a dangerous procedure in and of itself." Navy corpsmen could use the CMD program to effectively decide when to move the patient. Moeller adds that the Navy is also considering using a variation of the program for chest pain and major behavioral disorders.

The only other general type of CMD system currently in use is almost the complete opposite of de Dombal's knowledge-based system: It covers a huge range of medical problems but uses no complicated statistical analyses to serve up probabilities of certain conditions or diseases. Such a system simply stores and retrieves huge bodies of text, allowing overburdened practitioners to deal with an "information explosion."

Handling the 'Information Explosion'

The National Library of Medicine, Bethesda, Md, for example, has developed a prototypical Hepatitis Knowledge Base that is in use. The

American Medical Association and General Telephone and Electronics (GTE), moreover, will inaugurate the first nationwide electronic medical-health information system by late 1982. The program consists of a series of different data bases, some of which are closer to completion than others.

The drug data base in particular seems almost ready, according to Dan Harris, director of the Medical Information Network at the AMA. To use this data base, the physician might type "Valium" into his office computer terminal (which can be hooked up to the GTE network). He then would receive a kind of "menu" that would allow him to choose the kinds of information he would like, for example, on contraindications, pharmacokinetics, and drug interactions. Depending on the information requested, the computer will respond with information within seconds.

A disease data base, taken largely from the AMA's Current Medical Information and Terminology (CMIT), is under consideration now and would offer information on signs and symptoms, etiology, synonyms, and laboratory and pathology data for a named disease.

"The computer can give this information more quickly than a reference book," contends Harris. "If you're a physician in an emergency room whose specialty happens to be surgery, and a patient walks in, you may first have to know what drugs he's involved with. If these drugs differ from those you normally prescribe, this system can give you what you need to know immediately."

Cost has been the traditional barrier to computer systems, but with increasingly common low-priced terminals, this barrier is on the way out. However, collecting a data base often takes years of time: Texts and journals have to be combed for information which then has to be reorganized; files have to be continually updated. For many experimental systems that combine huge data bases with complex programs and lofty aspirations, this lag time increases from years to decades.

"It's easy to get the impression from reading (Ref. journal) papers that the day is around the corner when all doctors will be getting expert consultation from computers," says Dana Ludwig, MD, of the University of California, San Francisco. "That's not really true. Work has been going on for 20 years now, and there are very few systems being used in day-to-day practice anywhere -- let alone in widespread use."

On the other hand, because computers don't forget, overlook, tire, or equivocate, research is proceeding apace. There are plenty of incomplete but promising systems in experimental use, most often by physicians with computer science experience of their own. Very generally, these knowledge-based systems can be divided into two divergent types: numerically based and artificial intelligence (AI) systems.

Experimental Systems

Many of the numerically based systems resemble de Dombal's in that they use a statistical rule like Bayes theorem to make decisions. Bayes theorem provides a means for calculating the probability of hypothesis A, given the probability of hypothesis B. In medical terms, the theorem can be used to calculate the probability of each possible disease given a description of a particular case.

One major problem of these Bayesian systems is that they must make assumptions that simply do not hold true in real medicine. Bayes theorem, as generally used, "doesn't conveniently allow for the hypothesis of multiple diseases in the same patient," says Ludwig. Moreover, "it doesn't conveniently allow the representation of nonindependence of symptoms within the disease."

In other words, most CMD systems using Bayes theorem define certain entities as patient attributes and other entities as disease hypotheses. They assume that the patient can have only one disease and that, assuming he has it, all the attributes -- signs or symptoms -- occur independently of each other. Ludwig's INFERNET system tries to avoid these obvious oversimplifications by applying an extension of Bayes theorem to a network of interconnected diseases, symptoms, and signs.

"This system," explains Ludwig, "allows the possibility of intermediate states. For example, the disease of interest might be myocardial infarction, and it might be causing shortness of breath and high pulmonary wedge pressure. But actually it causes shortness of breath and pressure through an intermediate stage -- congestive heart failure. It's this intermediate state that links the two symptoms together." INFERNET can

take this link into account to give a more flexible and realistic picture of probabilities.

But INFERNET, like most other statistical-inference CMD systems, is nowhere near ready for clinical use. Not only must a vast amount of data be collected, but probabilities of specific diseases must be calculated -- a time-consuming and expensive project. Beyond that, the questions remain: Do complex statistical calculations really model or surpass medical reasoning in terms of efficacy? Can the probabilities cranked out of the computer make any difference in patient care?

Many physicians and computer specialists think not and have turned instead to that branch of computer science that attempts to simulate human reasoning: AI. Definitions of AI seem almost as plentiful as CMD systems, but generally AI can be defined as a type of program that generally manipulates ideas and symptoms rather than numbers.

Artificial Intelligence Systems

"The only way people would be willing to use (a typical statistical) program is if they were willing to turn over the decision to the computer," says Edward H. Shortliffe, MD, PhD, assistant professor of medicine and computer science at Stanford University. "And I don't think doctors are likely to do that -- ever -- for a real patient If you run a program and it says your patient has systemic lupus, probability .89, then what do you do? You have no way of deciding if, in fact, the computer used the information properly or improperly. And although the computer may have asked very reasonable questions about signs and symptoms, how it came up with that number and whether or not you should believe it is another issue."

Shortliffe and other people working in AI believe that physicians should be able to evaluate the computer's reasoning and make conclusions as to the validity of its decision. Therefore, instead of building a complex, unintuitive formula into the machine, they try to model their systems on human cognition. The problem, of course, is that they first must learn how human cognition works.

Part of this problem is being solved in the new field of medical decision making. Many CMD researchers -- both in AI and other areas -- are involved in the Society for Medical Decision Making and its international journal. One of the theories coming out of recent research, according to de Dombal (Nyhus LM: Computers and the surgeon. Surg Annual 1979; 2: 33-57), is that when physicians make decisions they acquire information, analyze it, and then decide the best course of management for the individual patient.

These decisions can be either "algorithmic" -- as when a physician draws together many pieces of clinical data to arrive at a diagnosis -- or "heuristic" -- as when a physician asks a few questions, quickly thinks of a likely diagnosis, and switches to specific questions that will confirm or refute that diagnosis. A third type of decision -- a more pragmatic one -- is called "payoff": here the physician asks questions that will help him determine patient management.

According to de Dombal, junior physicians and nonurgent problems usually evoke algorithmic decisions, while more senior physicians and urgent problems evoke heuristic and payoff approaches. Programs aiming to simulate the reasoning of an expert clinician, then, might follow a heuristic pathway.

While building AI systems, researchers discover additional information about human cognition, which they add to later versions of their systems. Shortliffe worked essentially on a trial-and-error basis for his first system, MYCIN, as well as his current system, ONCOCIN. For example, he would run MYCIN on what he knew to be a meningitis case and see that the system performed poorly. He would then analyze its "reasoning" sequence to see where it went wrong and modify the program until it yielded a reasonable recommendation.

According to Shortliffe, trial-and-error is "easier than asking an expert for everything he knows about meningitis and writing it down. It's very hard for people to analyze their own knowledge." One of ONCOCIN's major purposes is to extend basic knowledge about decision making and AI.

Its other purpose is to develop a clinically useful oncology consultation system that can explain its reasoning to the physician. ONCOCIN was implemented in 1981 for experimental use in patients with

lymphoma, and Shortliffe hopes to expand the program to therapies of many other cancers. By storing lengthy and complex protocols in the computer memory, he hopes to use ONCOCIN to greatly improve patient care and eliminate departures from protocol guidelines.

Like its predecessor MYCIN, ONCOCIN bases its decisions on a series of "if-then" rules. Depending on answers to the "if" condition, provided by the physician, the computer uses its preprogrammed "then" response as the "if" condition for the next rule. An English "translation" of the rule for determining "attenuated dose" is:

RULE 075

To determine the current attenuated dose for all drugs in MOPP (nitrogen mustard, Oncovin, procarbazine, prednisone) or for all drugs in PAVE (procarbazine, Adriamycin, and Velban)

If: (1) This is the start of the first cycle after a cycle was aborted, and

(2) The blood counts do not warrant dose attenuation

Then: Conclude that the current dose is 75% of the previous dose.

ONCOCIN also draws on stored data files containing attributes of other patients as well as rules about drug usage, tests, and other information relevant for protocol decision making. Combining this entire knowledge base with information about the new patient's diagnosis and test results, ONCOCIN produces a recommendation, along with an explanation of its decision, about five minutes after the physician starts entering data.

Another experimental system using AI, but for a much larger area of medicine, is CADUCEUS (formerly INTERNIST) at the University of Pittsburgh. The program, supported by the National Institutes of Health and the National Library of Medicine, initially was limited to internal medicine but is currently branching out to pediatrics and neurology. It contains "semiquantitative" information about frequencies of various manifestations and how strongly one manifestation indicates one disease. Designed to guide physicians confronted with difficult diagnostic problems, CADUCEUS currently has a **knowledge base** of more than 600 diseases.

"If you put this all together, you've got a knowledge base in internal medicine alone that is many times what the human brain could possibly remember," says Jack Myers, MD, professor-at-large (medicine) at the University of Pittsburgh. "I've built the thing, and I can't remember the data!"

Myers, who constructed CADUCEUS with Harry E. Pople, PhD, associate professor of business administration at Pittsburgh, has been practicing internal medicine since the late 1930s. In the early 1970s, he began looking for a way to pass on his accumulated experience. "Rather than try to write another textbook, I figured it'd be better to try to put this into a computer where it could be manipulated and used," he says. He actually sought out computer scientists and interested them in his project.

In keeping with its origins, CADUCEUS serves as an expert consultant offering a learned opinion that the physician "can take or leave," says Myers. For example, a physician may complete a physical examination and find a certain kind of heart murmur. That kind of heart murmur occurs in the descriptions of six diseases. The system draws these six out, along with "perfect descriptions" for all.

Myers further explains that there are two numbers associated with heart murmur. The first one tells the likelihood of certain diseases given the heart murmur alone. The second number tells the likelihood of this heart murmur, given certain diseases. In reality, of course, there are many more pieces of information than "heart murmur," but the basic process remains comparable: The computer comes up with the most likely diagnosis on the basis of these numbers.

"The machine sets up a hypothesis for each disease and can rank its probability by comparing the known information to its ideal model," says Myers. One big asset is flexibility. "In real life you rarely see a patient with every manifestation. And, like the human brain, CADUCEUS weighs probabilities between less-than-ideal descriptions." If the information given by the physician hasn't been sufficient for a conclusive diagnosis, CADUCEUS moves into an interrogative phase and asks for precise pieces of information.

Why the Slow Growth of CMD?

Although clinicians associated with the University of Pittsburgh often

use CADUCEUS, both this system and ONCOCIN are far from routine use or widespread marketing. One problem is the incomplete knowledge base. "We cannot put the system out for routine use until those unknown diseases are fitted in -- in case the patient is unlucky enough to have one of those," stresses Myers. "The next best fit isn't acceptable,"

Technology presents another problem. Although both Shortliffe and Myers are confident that these problems will disappear within the next decade, there is presently no small and affordable computer that can handle the typical AI program.

Shortliffe goes even further in his reservations. "I don't think there is a recent decision-making system available to run on any computer that a physician would want to use on a regular basis," he says. Although not all workers in the field would agree, they can hardly deny that one or two routinely used systems for 20 years of research is not a good record.

Technological limitations plague even investigators working on other than AI systems. "It's simply not true that computers can do everything," Ludwig emphasizes. "If you wanted to write a perfect program to play chess, it would have to look at every possible move and every possible sequence of moves at any given board position. That's something the fastest computers couldn't handle from now until hell freezes over." Since a perfect program is not possible, for either a chess program or a medical decision, choices of possibilities must be limited; how to do this is not at all clear.

Poorly defined medical terminology and the uncertainty of medical knowledge itself are other bottlenecks for CMD systems, Ludwig says. Furthermore, notes Myers, computers still are not good at interpreting often crucial changes in patient attributes or laboratory values over time.

But even without these limitations, the real difficulty has been physician acceptance, which has been withheld for much more than technical reasons.

For one thing, if the decisions are useless, physicians won't rely on them -- no matter how technically accurate they may be. According to Friedman, who has been working with CMD systems for more than a decade and believes strongly in their ultimate value, many of the programs make decisions that no one needs to make.

Above all, he questions using computers for diagnostic decisions. "There are very few difficult decisions in medicine. The difficult decisions are the ones that don't fit the prior mold anyway, the ones that you don't have the data to base the decisions on in the first place." Most programs end up telling the physician what he knew to begin with.

The really valuable system, contends Friedman, would decide what additional tests or questions would aid the physician's diagnosis and suggest them. "If we could use the computer to make good clinical decisions, then we could begin to talk about a diagnosis," he says. "The real questions are whether to do a test, whether it's cost effective, what is the real mortality, how effective is the therapy."

One program that at least begins to answer these questions is the Present Illness Program (PIP) at Massachusetts Institute of Technology, Cambridge, and Tufts University, Medford, Mass. An AI program concerning edema, PIP simulates an expert taking a case history, thus suggesting important issues to less-expert physicians. "PIP won't outperform experts," acknowledges Stephen G. Pauker, MD, associate professor of medicine and chief of the position of clinical decision making at Tufts-New England Medical Center. "But most physicians aren't experts."

For a patient initially seen with massive pedal edema, PIP might ask: "Is pedal edema, which is massive, (Ref. lastig) (1) for days? (2) for weeks? (3) for months? (4) for years?" The physician responds and another multiple-choice question appears: "Is it (1) first time? (2) infrequent? (3) occasional? (4) frequent?" Depending on the responses, PIP might ask later about temporal patterns, symmetry, pain, and dyspnea, as well as about the patient's alcohol consumption, life insurance, and military history.

The result is a literate paragraph summarizing the case and offering several diagnostic hypotheses (see figures, previous page).

Most researchers defend the usefulness of large knowledge bases in general, whether or not they suggest further tests or questions. As Marsden Blois, MD, professor of medical information science at the University of California, San Francisco, points out, "If the physician does not think of the correct diagnosis, he can't make it. A useful system can offer a menu

or list of things that he might want to think about in face of a difficult diagnostic problem -- like an uncommon disease that he may never have seen in his whole experience and may never have thought of since medical school." Blois' RECONSIDER serves this function by generating a differential diagnosis, based on the CMIT, given a list of patient findings.

Usefulness can also depend on the demographic situation. "If you're in a tertiary care center where there are consultants all over the place, this kind of program may be less useful than in a rural area or medically underserved area," says Shortliffe.

Even if the programs are useful, however, physicians may be intimidated by unfamiliar computer languages. Most of the people building today's CMD systems take what they call the "user-interface" problem into account but, according to James A. Reggia, MD, PhD, most don't go far enough. Reggia, an assistant professor of neurology and mathematics at the University of Maryland, has designed what he calls a "knowledge Management System" (KMS) to obviate this problem.

A KMS does not actually contain a knowledge base like CMD systems, but provides a framework into which a physician-author can insert his own knowledge base. It contains a collection of inference mechanisms (eg, Bayesian strategies or hypothesize-and-test models of diagnostic reasoning) that can operate on the new data. Because KMS uses a simple, "almost English" language, it allows a physician to implement a system specifically useful to him.

"Some people think that our idea is crazy," says Reggia. "They think we'll never get physicians to be able to program computers. I don't believe so."

To prove his point, Reggia and colleagues gave about 4k medical students a course on the system and taught them how to build their own CMD systems. The students constructed a statistical pattern classification for thyroid diagnosis, for example, and a logical rule-based system to classify lung cancer. Regardless of past computer experience, students quickly and easily mastered the system.

A less remediable problem may be what Shortliffe has called the almost "visceral" reaction to anything related to computers. But familiarity seems to be quickly wiping out most objections. Not only are computers becoming part of daily life, but costs continue to fall. Moreover, students coming into and finishing medical school frequently have computer experience, and many physicians have office computers that could easily accommodate CMD systems.

Above all, as an increasing number of physicians begin to see computers as useful tools rather than threatening replacements, hostility is declining. "If a doctor wants to analyze the blood," explains de Dombal, "he doesn't go and sniff it himself: he uses a machine. And if he wants to know whether the bones are broken, he doesn't go feel them out for himself: he uses an X-ray machine. Now, for the first time, he can actually use a machine to help him with the symptoms as well; the computer decision is simply another piece of evidence."

At the heart of the matter lies the question of whether a physician with this computer assistance generates significantly better patient care than a physician without it. For the most part, researchers have not yet answered this question.

"Physicians are not stick-in-the-muds," stresses Friedman. "It's ridiculous to say they won't use computers. They use laser beams, they buy CT scanners for a million bucks apiece When these decision systems can do something that doctors can't do, every doctor will have one."

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or Kaiser Industries. The Foundation supports research in four main areas: health policy, reproductive health, HIV policy, and health and development in South Africa. The Foundation also maintains a special interest in health policy and innovation in its home state of California.

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Computer-assisted medical decision-making: interest growing (MEDICAL NEWS
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Computers can never replace physicians. Only physicians have the ability to reason logically and to mix that reason with intuition, experience, and ethics -- something no machine can ever learn to do."

Or so many physicians have been telling people proposing computer-assisted medical decision making (CMD) since the early 1960s, and controversy has continued. But now it looks like the two sides are nearing agreement: Computers may never replace physicians, but they can and will assist their decisions.

"Assist" is the key word in CMD. Early advocates tended to overestimate the powers of the computer and promised complete clinical evaluation at the push of a button. It was natural for physicians to feel somewhat threatened. It was also natural that, with experience, such promises had to be modified.

Today there still are only several functioning knowledge-based decision systems -- called "knowledge-based" because they make inferences using a data base of medical information stored in a computer's memory -- and they are extremely modest. More complex systems are currently under development, but even these will merely serve as expert consultants; the ultimate decision, which requires personal, occasionally subjective considerations, still will rest with the practitioner.

"The early systems attempted to do diagnosis for the doctors -- which is crazy," says Francis T. de Dombal, MB, MD, consultant with the Leeds Area Health Authority and Reader in Clinical Information Science at the University of Leeds, England. "Doctors do some things very well indeed, and computers do them very badly. For example, if the Leeds United Football Team was playing at home, there'd be quite a lot of people with bellyaches. The experienced doctor would know the source of all these bellyaches, and he wouldn't take everyone's appendix out. The computer might well do so."

de Dombal is well acquainted with the abilities and limitations of computers: His Leeds system was one of the first and remains one of the few fully operative CMD systems. Able to discriminate between common causes of acute abdominal pain, the system has been used for the past eight years in three United Kingdom (UK) hospitals, and recently the UK government authorized and funded a three-year trial in 11 other hospitals.

Although both the problem and the possible diagnoses are limited, the system has improved diagnostic accuracy for abdominal pain by 20%, according to de Dombal. After studying the pattern of admittances in his own hospital and others, he and his team constructed probabilities of common causes of abdominal pain and entered these into the computer memory along with the signs and symptoms associated with each cause.

'What Have I Got, Doc?'

When a patient is initially seen with abdominal pain, the examining physician records observations on a preprinted form that requests information about the pain, other symptoms, medical history, and findings from the general examination. The physician then gives the form to a member of the computing team, who enters it into the computer by choosing an "answer" for each of a series of categories. For example, under the category of "relieving factors," he can choose between "lying still," "vomiting," "antacids," "food," "other," and "nil." Other categories include sex, age, site of pain at onset, aggravating factors, and site of pain at present.

Next the computer analyzes the data. Essentially, it compares the

details of the new case with those of hundreds of similar cases in its memory and uses a theory of probabilities to calculate the likelihood of various diagnoses. The resulting printout displayed to the physician lists all the symptoms and gives the probabilities that the patient has appendicitis, non-specific abdominal pain, diverticular disease, perforated peptic ulcer, cholecystitis, small bowel obstruction, or pancreatitis. A sample printout might suggest a 27.11% chance of appendicitis, a 12.28% chance of perforated peptic ulcer, and a 60.60% chance of nonspecific abdominal pain; the practitioner can combine this information with his clinical impressions to arrive at a diagnosis.

"I would defend to the death the doctor's right to override what comes out of the computer if he thinks it's crazy," stresses de Dombal. "Right across the top of all our systems it says, 'Clinical judgment must take precedence; these are only suggestions.'"

After testing the system from January 1971 to August 1972, de Dombal found that preoperative diagnoses made with the computer-aided system (using data provided by the registrar) were 91% correct. This was in comparison with 42% correct for diagnoses made by unaided admitting physicians, 71% correct for diagnoses made by unaided house surgeons (less than six months experience), 79% correct diagnoses by unaided registrars (between one and two years surgical experience), and 81% correct diagnoses by unaided senior clinicians (more than five years surgical experience). These results show one obvious advantage of the system: training inexperienced physicians.

"What we're really trying to do," says de Dombal, "is to get the inexperienced doctor's level of performance up to that of the senior clinicians within a few weeks, as opposed to ten years."

The improvement figures may be misleading, however, since the physician often makes the crucial decision before turning to the computer.

"Before these trials were run," says Richard Bruce Friedman, MD, associate professor of medicine and human oncology at the University of Wisconsin Medical School, Madison, "the investigators had already screened out every area but abdominal pain. By the time (Ref. aphysicia) knows it's abdominal pain, he calls the surgeon and he gets an x-ray -- even without a computer. The test is an artificial situation and makes no real difference to clinical procedure.

"Even if you send this program neck pain, it will still make a diagnosis of abdominal pain."

It seems to make a difference to some physicians, though. With the help of the World Organization of Gastroenterology, investigators have modified the data base to take geographical variation into account, as abdominal pain may have different causes in different areas. And since 1972, the cost of the program has come down considerably: Once run on a large university computer, it now can run on small computers like Pets and Apples, which are quite common in hospitals and physicians' offices these days.

Moreover, the US Navy is currently evaluating de Dombal's program for use on submarines and is adapting the data base to this population. According to George Moeller, MD, director of the Behavioral Sciences Branch of the US Navy, appendicitis is one of the principal medical problems aboard submarines. Although some medical problems can be handled aboard, surgery of course requires moving the patient off the submarine.

"That's something we would like to avoid," says Moeller, "not only because it (Ref. movigthepatiet) would interrupt the mission but because it's a dangerous procedure in and of itself." Navy corpsmen could use the CMD program to effectively decide when to move the patient. Moeller adds that the Navy is also considering using a variation of the program for chest pain and major behavioral disorders.

The only other general type of CMD system currently in use is almost the complete opposite of de Dombal's knowledge-based system: It covers a huge range of medical problems but uses no complicated statistical analyses to serve up probabilities of certain conditions or diseases. Such a system simply stores and retrieves huge bodies of text, allowing overburdened practitioners to deal with an "information explosion."

Handling the 'Information Explosion'

The National Library of Medicine, Bethesda, Md, for example, has developed a prototypical Hepatitis Knowledge Base that is in use. The

American Medical Association and General Telephone and Electronics (GTE), moreover, will inaugurate the first nationwide electronic medical-health information system by late 1982. The program consists of a series of different data bases, some of which are closer to completion than others.

The drug data base in particular seems almost ready, according to Dan Harris, director of the Medical Information Network at the AMA. To use this data base, the physician might type "Valium" into his office computer terminal (which can be hooked up to the GTE network). He then would receive a kind of "menu" that would allow him to choose the kinds of information he would like, for example, on contraindications, pharmacokinetics, and drug interactions. Depending on the information requested, the computer will respond with information within seconds.

A disease data base, taken largely from the AMA's Current Medical Information and Terminology (CMIT), is under consideration now and would offer information on signs and symptoms, etiology, synonyms, and laboratory and pathology data for a named disease.

"The computer can give this information more quickly than a reference book," contends Harris. "If you're a physician in an emergency room whose specialty happens to be surgery, and a patient walks in, you may first have to know what drugs he's involved with. If these drugs differ from those you normally prescribe, this system can give you what you need to know immediately."

Cost has been the traditional barrier to computer systems, but with increasingly common low-priced terminals, this barrier is on the way out. However, collecting a data base often takes years of time: Texts and journals have to be combed for information which then has to be reorganized; files have to be continually updated. For many experimental systems that combine huge data bases with complex programs and lofty aspirations, this lag time increases from years to decades.

"It's easy to get the impression from reading (Ref. journal) papers that the day is around the corner when all doctors will be getting expert consultation from computers," says Dana Ludwig, MD, of the University of California, San Francisco. "That's not really true. Work has been going on for 20 years now, and there are very few systems being used in day-to-day practice anywhere -- let alone in widespread use."

On the other hand, because computers don't forget, overlook, tire, or equivocate, research is proceeding apace. There are plenty of incomplete but promising systems in experimental use, most often by physicians with computer science experience of their own. Very generally, these knowledge-based systems can be divided into two divergent types: numerically based and artificial intelligence (AI) systems.

Experimental Systems

Many of the numerically based systems resemble de Dombal's in that they use a statistical rule like Bayes theorem to make decisions. Bayes theorem provides a means for calculating the probability of hypothesis A, given the probability of hypothesis B. In medical terms, the theorem can be used to calculate the probability of each possible disease given a description of a particular case.

One major problem of these Bayesian systems is that they must make assumptions that simply do not hold true in real medicine. Bayes theorem, as generally used, "doesn't conveniently allow for the hypothesis of multiple diseases in the same patient," says Ludwig. Moreover, "it doesn't conveniently allow the representation of nonindependence of symptoms within the disease."

In other words, most CMD systems using Bayes theorem define certain entities as patient attributes and other entities as disease hypotheses. They assume that the patient can have only one disease and that, assuming he has it, all the attributes -- signs or symptoms -- occur independently of each other. Ludwig's INFERNET system tries to avoid these obvious oversimplifications by applying an extension of Bayes theorem to a network of interconnected diseases, symptoms, and signs.

"This system," explains Ludwig, "allows the possibility of intermediate states. For example, the disease of interest might be myocardial infarction, and it might be causing shortness of breath and high pulmonary wedge pressure. But actually it causes shortness of breath and pressure through an intermediate stage -- congestive heart failure. It's this intermediate state that links the two symptoms together." INFERNET can

take this link into account to give a more flexible and realistic picture of probabilities.

But INFERNET, like most other statistical-inference CMD systems, is nowhere near ready for clinical use. Not only must a vast amount of data be collected, but probabilities of specific diseases must be calculated -- a time-consuming and expensive project. Beyond that, the questions remain: Do complex statistical calculations really model or surpass medical reasoning in terms of efficacy? Can the probabilities cranked out of the computer make any difference in patient care?

Many physicians and computer specialists think not and have turned instead to that branch of computer science that attempts to simulate human reasoning: AI. Definitions of AI seem almost as plentiful as CMD systems, but generally AI can be defined as a type of program that generally manipulates ideas and symptoms rather than numbers.

Artificial Intelligence Systems

"The only way people would be willing to use (a typical statistical) program is if they were willing to turn over the decision to the computer," says Edward H. Shortliffe, MD, PhD, assistant professor of medicine and computer science at Stanford University. "And I don't think doctors are likely to do that -- ever -- for a real patient If you run a program and it says your patient has systemic lupus, probability .89, then what do you do? You have no way of deciding if, in fact, the computer used the information properly or improperly. And although the computer may have asked very reasonable questions about signs and symptoms, how it came up with that number and whether or not you should believe it is another issue."

Shortliffe and other people working in AI believe that physicians should be able to evaluate the computer's reasoning and make conclusions as to the validity of its decision. Therefore, instead of building a complex, unintuitive formula into the machine, they try to model their systems on human cognition. The problem, of course, is that they first must learn how human cognition works.

Part of this problem is being solved in the new field of medical decision making. Many CMD researchers -- both in AI and other areas -- are involved in the Society for Medical Decision Making and its international journal. One of the theories coming out of recent research, according to de Dombal (Nyhuis LM: Computers and the surgeon. Surg Annual 1979; 2: 33-57), is that when physicians make decisions they acquire information, analyze it, and then decide the best course of management for the individual patient.

These decisions can be either "algorithmic" -- as when a physician draws together many pieces of clinical data to arrive at a diagnosis -- or "heuristic" -- as when a physician asks a few questions, quickly thinks of a likely diagnosis, and switches to specific questions that will confirm or refute that diagnosis. A third type of decision -- a more pragmatic one -- is called "payoff": here the physician asks questions that will help him determine patient management.

According to de Dombal, junior physicians and nonurgent problems usually evoke algorithmic decisions, while more senior physicians and urgent problems evoke heuristic and payoff approaches. Programs aiming to simulate the reasoning of an expert clinician, then, might follow a heuristic pathway.

While building AI systems, researchers discover additional information about human cognition, which they add to later versions of their systems. Shortliffe worked essentially on a trial-and-error basis for his first system, MYCIN, as well as his current system, ONCOCIN. For example, he would run MYCIN on what he knew to be a meningitis case and see that the system performed poorly. He would then analyze its "reasoning" sequence to see where it went wrong and modify the program until it yielded a reasonable recommendation.

According to Shortliffe, trial-and-error is "easier than asking an expert for everything he knows about meningitis and writing it down. It's very hard for people to analyze their own knowledge." One of ONCOCIN's major purposes is to extend basic knowledge about decision making and AI.

Its other purpose is to develop a clinically useful oncology consultation system that can explain its reasoning to the physician. ONCOCIN was implemented in 1981 for experimental use in patients with

lymphoma, and Shortliffe hopes to expand the program to therapies of many other cancers. By storing lengthy and complex protocols in the computer memory, he hopes to use ONCOCIN to greatly improve patient care and eliminate departures from protocol guidelines.

Like its predecessor MYCIN, ONCOCIN bases its decisions on a series of "if-then" rules. Depending on answers to the "if" condition, provided by the physician, the computer uses its preprogrammed "then" response as the "if" condition for the next rule. An English "translation" of the rule for determining "attenuated dose" is:

RULE 075

To determine the current attenuated dose for all drugs in MOPP (nitrogen mustard, Oncovin, procarbazine, prednisone) or for all drugs in PAVE (procarbazine, Adriamycin, and Velban)

If: (1) This is the start of the first cycle after a cycle was aborted, and

(2) The blood counts do not warrant dose attenuation

Then: Conclude that the current dose is 75% of the previous dose.

ONCOCIN also draws on stored data files containing attributes of other patients as well as rules about drug usage, tests, and other information relevant for protocol decision making. Combining this entire knowledge base with information about the new patient's diagnosis and test results, ONCOCIN produces a recommendation, along with an explanation of its decision, about five minutes after the physician starts entering data.

Another experimental system using AI, but for a much larger area of medicine, is CADUCEUS (formerly INTERNIST) at the University of Pittsburgh. The program, supported by the National Institutes of Health and the National Library of Medicine, initially was limited to internal medicine but is currently branching out to pediatrics and neurology. It contains "semiquantitative" information about frequencies of various manifestations and how strongly one manifestation indicates one disease. Designed to guide physicians confronted with difficult diagnostic problems, CADUCEUS currently has a knowledge base of more than 600 diseases.

"If you put this all together, you've got a knowledge base in internal medicine alone that is many times what the human brain could possibly remember," says Jack Myers, MD, professor-at-large (medicine) at the University of Pittsburgh. "I've built the thing, and I can't remember the data!"

Myers, who constructed CADUCEUS with Harry E. Pople, PhD, associate professor of business administration at Pittsburgh, has been practicing internal medicine since the late 1930s. In the early 1970s, he began looking for a way to pass on his accumulated experience. "Rather than try to write another textbook, I figured it'd be better to try to put this into a computer where it could be manipulated and used," he says. He actually sought out computer scientists and interested them in his project.

In keeping with its origins, CADUCEUS serves as an expert consultant offering a learned opinion that the physician "can take or leave," says Myers. For example, a physician may complete a physical examination and find a certain kind of heart murmur. That kind of heart murmur occurs in the descriptions of six diseases. The system draws these six out, along with "perfect descriptions" for all.

Myers further explains that there are two numbers associated with heart murmur. The first one tells the likelihood of certain diseases given the heart murmur alone. The second number tells the likelihood of this heart murmur, given certain diseases. In reality, of course, there are many more pieces of information than "heart murmur," but the basic process remains comparable: The computer comes up with the most likely diagnosis on the basis of these numbers.

"The machine sets up a hypothesis for each disease and can rank its probability by comparing the known information to its ideal model," says Myers. One big asset is flexibility. "In real life you rarely see a patient with every manifestation. And, like the human brain, CADUCEUS weighs probabilities between less-than-ideal descriptions." If the information given by the physician hasn't been sufficient for a conclusive diagnosis, CADUCEUS moves into an interrogative phase and asks for precise pieces of information.

Why the Slow Growth of CMD?

Although clinicians associated with the University of Pittsburgh often

use CADUCEUS, both this system and ONCOCIN are far from routine use or widespread marketing. One problem is the incomplete knowledge base. "We cannot put the system out for routine use until those unknown diseases are fitted in -- in case the patient is unlucky enough to have one of those," stresses Myers. "The next best fit isn't acceptable,"

Technology presents another problem. Although both Shortliffe and Myers are confident that these problems will disappear within the next decade, there is presently no small and affordable computer that can handle the typical AI program.

Shortliffe goes even further in his reservations. "I don't think there is a recent decision-making system available to run on any computer that a physician would want to use on a regular basis," he says. Although not all workers in the field would agree, they can hardly deny that one or two routinely used systems for 20 years of research is not a good record.

Technological limitations plague even investigators working on other than AI systems. "It's simply not true that computers can do everything," Ludwig emphasizes. "If you wanted to write a perfect program to play chess, it would have to look at every possible move and every possible sequence of moves at any given board position. That's something the fastest computers couldn't handle from now until hell freezes over." Since a perfect program is not possible, for either a chess program or a medical decision, choices of possibilities must be limited; how to do this is not at all clear.

Poorly defined medical terminology and the uncertainty of medical knowledge itself are other bottlenecks for CMD systems, Ludwig says. Furthermore, notes Myers, computers still are not good at interpreting often crucial changes in patient attributes or laboratory values over time.

But even without these limitations, the real difficulty has been physician acceptance, which has been withheld for much more than technical reasons.

For one thing, if the decisions are useless, physicians won't rely on them -- no matter how technically accurate they may be. According to Friedman, who has been working with CMD systems for more than a decade and believes strongly in their ultimate value, many of the programs make decisions that no one needs to make.

Above all, he questions using computers for diagnostic decisions. "There are very few difficult decisions in medicine. The difficult decisions are the ones that don't fit the prior mold anyway, the ones that you don't have the data to base the decisions on in the first place." Most programs end up telling the physician what he knew to begin with.

The really valuable system, contends Friedman, would decide what additional tests or questions would aid the physician's diagnosis and suggest them. "If we could use the computer to make good clinical decisions, then we could begin to talk about a diagnosis," he says. "The real questions are whether to do a test, whether it's cost effective, what is the real mortality, how effective is the therapy."

One program that at least begins to answer these questions is the Present Illness Program (PIP) at Massachusetts Institute of Technology, Cambridge, and Tufts University, Medford, Mass. An AI program concerning edema, PIP simulates an expert taking a case history, thus suggesting important issues to less-expert physicians. "PIP won't outperform experts," acknowledges Stephen G. Pauker, MD, associate professor of medicine and chief of the position of clinical decision making at Tufts-New England Medical Center. "But most physicians aren't experts."

For a patient initially seen with massive pedal edema, PIP might ask: "Is pedal edema, which is massive, (Ref. lastig) (1) for days? (2) for weeks? (3) for months? (4) for years?" The physician responds and another multiple-choice question appears: "Is it (1) first time? (2) infrequent? (3) occasional? (4) frequent?" Depending on the responses, PIP might ask later about temporal patterns, symmetry, pain, and dyspnea, as well as about the patient's alcohol consumption, life insurance, and military history.

The result is a literate paragraph summarizing the case and offering several diagnostic hypotheses (see figures, previous page).

Most researchers defend the usefulness of large knowledge bases in general, whether or not they suggest further tests or questions. As Marsden Blois, MD, professor of medical information science at the University of California, San Francisco, points out, "If the physician does not think of the correct diagnosis, he can't make it. A useful system can offer a menu

or list of things that he might want to think about in face of a difficult diagnostic problem -- like an uncommon disease that he may never have seen in his whole experience and may never have thought of since medical school." Blois' RECONSIDER serves this function by generating a differential diagnosis, based on the CMIT, given a list of patient findings.

Usefulness can also depend on the demographic situation. "If you're in a tertiary care center where there are consultants all over the place, this kind of program may be less useful than in a rural area or medically underserved area," says Shortliffe.

Even if the programs are useful, however, physicians may be intimidated by unfamiliar computer languages. Most of the people building today's CMD systems take what they call the "user-interface" problem into account but, according to James A. Reggia, MD, PhD, most don't go far enough. Reggia, an assistant professor of neurology and mathematics at the University of Maryland, has designed what he calls a "knowledge Management System" (KMS) to obviate this problem.

A KMS does not actually contain a knowledge base like CMD systems, but provides a framework into which a physician-author can insert his own knowledge base. It contains a collection of inference mechanisms (eg, Bayesian strategies or hypothesize-and-test models of diagnostic reasoning) that can operate on the new data. Because KMS uses a simple, "almost English" language, it allows a physician to implement a system specifically useful to him.

"Some people think that our idea is crazy," says Reggia. "They think we'll never get physicians to be able to program computers. I don't believe so."

To prove his point, Reggia and colleagues gave about 4k medical students a course on the system and taught them how to build their own CMD systems. The students constructed a statistical pattern classification for thyroid diagnosis, for example, and a logical rule-based system to classify lung cancer. Regardless of past computer experience, students quickly and easily mastered the system.

A less remediable problem may be what Shortliffe has called the almost "visceral" reaction to anything related to computers. But familiarity seems to be quickly wiping out most objections. Not only are computers becoming part of daily life, but costs continue to fall. Moreover, students coming into and finishing medical school frequently have computer experience, and many physicians have office computers that could easily accommodate CMD systems.

Above all, as an increasing number of physicians begin to see computers as useful tools rather than threatening replacements, hostility is declining. "If a doctor wants to analyze the blood," explains de Dombal, "he doesn't go and sniff it himself: he uses a machine. And if he wants to know whether the bones are broken, he doesn't go feel them out for himself: he uses an X-ray machine. Now, for the first time, he can actually use a machine to help him with the symptoms as well; the computer decision is simply another piece of evidence."

At the heart of the matter lies the question of whether a physician with this computer assistance generates significantly better patient care than a physician without it. For the most part, researchers have not yet answered this question.

"Physicians are not stick-in-the-muds," stresses Friedman. "It's ridiculous to say they won't use computers. They use laser beams, they buy CT scanners for a million bucks apiece When these decision systems can do something that doctors can't do, every doctor will have one."

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DXplain; An Evolving Diagnostic Decision-Support System (SPECIAL COMMUNICATIONS)

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ABSTRACT: DXplain is an evolving computer-based diagnostic decision-support system designed for use by the physician who has no computer expertise. DXplain accepts a list of clinical manifestations and then proposes diagnostic hypotheses. The program explains and justifies its interpretations and provides access to a knowledge base concerning the differential diagnosis of the signs and symptoms. DXplain was developed with the support and cooperation of the American Medical Association. The system is distributed to the medical community through AMA/NET -- a nationwide computer communications network sponsored by the American Medical Association -- and through the Massachusetts General Hospital Continuing Education Network. A key element in the distribution of DXplain is the planned collaboration with its physician-users whose comments, criticisms, and suggestions will play an important role in modifying and enhancing the knowledge base.

SHORTLIFFE (Ref. 1) defines a computer-based medical decision-support system as a computer program designed to help health professionals make clinical decisions. Under this broad definition, there are many decision-support systems in use today. They include such applications as clinical laboratory systems, pharmacy systems, and radiology reporting systems. For the most part, these are "passive" information management tools. That is, they make information more readily available to the physician but they do not provide "active" decision support by applying medical knowledge to a specific patient's data, nor do they recommend a specific conclusion or course of action.

There has been less success in developing active systems. One strategy used in such systems applies predefined rules to the patient's data and alerts providers to conditions that might require action. The most successful system for inpatient care is the HELP system. (Ref. 2) In ambulatory medicine, two examples of systems that provide patient-specific recommendations for ambulatory care are CARE (Ref. 3) and COSTAR. (Ref. 4) There are also a few examples of "expert" systems that guide the physician in treating certain complex, but well-defined, conditions, eg, the ONCOCIN system. (Ref. 5) These systems contain in-depth knowledge about a well-defined subset of medical knowledge and require considerable and detailed information about the patient's clinical status to provide the computer-generated consultations.

Computer-aided diagnosis in general medicine requires a much broader level of decision support. There have been a number of provocative research efforts in computer-aided diagnosis, (Ref. 6-9) but these have been research prototypes whose contributions were primarily methodological. With the exception of the work by deDombal et al, (Ref. 10) these programs were not made available to the practicing physician. There are a number of reasons to explain the limited impact of information technology in the diagnostic aspects of medical decision making. (Ref. 1,11,12) Major

problems have included difficulty in accessing and interacting with the systems, a limited area of application (eg, one of the most successful computer-aided diagnosis programs is limited to the differential diagnosis of the acute abdomen (Ref. 10)), a limited ability of the systems to explain and justify the interpretations, and less than acceptable quality of the interpretations. Some investigators believe that there are major intellectual and technical problems that must be solved before there can be a truly reliable consulting program. In particular, it is claimed that computer programs must be able to incorporate pathophysiological knowledge and causal relationship based on pathophysiological reasoning. (Ref. 12)

We accept the validity of these concerns, but take a more optimistic position concerning the potential for using currently available knowledge and technology to assist the physician in the information needs of daily practice. A recent study suggests that the information needs of physicians in office practice are not being met by printed sources such as textbooks and journal articles. (Ref. 13) Of the practice-related questions that were identified, 25% involved the diagnosis of symptoms, physical findings, or syndromes. We believe that a significant portion of the practical needs of clinical medicine can be met now by providing ready access to a computer-stored knowledge base of diagnoses and their associated signs and symptoms.

We believe it is possible to develop a computer program that uses an extensive knowledge base and relatively simple computational models to provide significant diagnostic problem-solving assistance to the practicing physician. The program should allow the computer-naive user to enter a set of signs and symptoms using a typical medical vocabulary. The program would then generate a list of hypotheses that deserve consideration, comment on the diagnostic relevance of each sign and symptom, and suggest specific additional data elements that might clarify the differential diagnosis currently favored by the computer model. (Ref. 9,14-16)

This article describes DXplain, an evolving computer-based diagnostic decision-support system designed for use by the physician who has no computer expertise. (Ref. 14) DXplain accepts a list of clinical manifestations and then proposes diagnostic hypotheses. DXplain explains and justifies its interpretations and provides easy access to a comprehensive knowledge base concerning the differential diagnosis of the set of signs and symptoms.

DXplain does not attempt to make a single diagnosis to mimic the behavior or replace the judgment of the expert clinician. DXplain has a less ambitious, but perhaps more attainable goal: to suggest a list of diagnoses that should be considered given a particular set of signs and symptoms. Because DXplain is in a continuing state of development, we have labeled it an evolving diagnostic decision-support system. Our plan is that DXplain will continue to improve through collaboration with its physician-users whose comments, criticisms, and suggestions will play an important role in modifying and enhancing the knowledge base and the algorithms used in the computer-generated interpretations.

SYSTEM CAPABILITIES

We believe that the following six criteria are important for a differential diagnosis decision-support system intended for use in routine clinical practice. The system should (1) be easy to use by physicians who have little or no computer background; (2) be based on comprehensive medical content; (3) provide correct and accurate interpretations; (4) justify its interpretations; (5) be convenient to access from the physician's office, hospital, or home; and (6) evolve and improve as a result of user criticism and analysis of user sessions.

Easy to Use

It has been the general experience that few practicing physicians will use computer programs requiring extensive training or knowledge of computer technology. DXplain demands little knowledge of computer technology and requires only the use of the vocabulary common in medical practice. On-line help is available for an explanation of the system commands.

As with any decision-support system, DXplain uses a controlled vocabulary for communicating patient information to the system. Computer technology has not yet progressed to the stage in which a computer program can recognize the free-form narrative text that a physician might use to

describe clinical manifestations in a medical record or with a colleague. The predefined medical vocabulary used by DXplain consists of more than 4700 terms based on the clinical and basic laboratory data that might be collected in an ambulatory practice or in the emergency department.

DXplain has several features that assist the user in selecting the desired terms from the controlled vocabulary. For instance, there is extensive synonym and abbreviation terminology; also, the system can recognize and correct many misspellings. DXplain can recognize terms that are "close" (eg, "congestive heart failure" and "heart failure"), as well as synonyms for terms at both the single-word level (eg, "kidney" and "renal" are equivalent in many different terms) and at the fullphrase level (eg, "anisocoria" is equivalent to "pupillary inequality," "factor VIII deficiency" is considered equivalent to "hemophilia"; and "blood glucose elevated" is considered equivalent to "hyperglycemia"). In addition, many abbreviations are recognized (eg, "ESR" and "CHF") to speed data entry.

The DXplain vocabulary structure is hierarchical, which allows flexibility in specifying the precise level of detail of the clinical manifestation. Thus, DXplain groups more specific terms (such as "lower abdominal pain") under a less specific term (such as "abdominal pain"). This hierarchy is important for both the user interface and the algorithm used for interpretation. When a user enters a specific term, such as "right lower quadrant pain," all of the appropriate less-specific terms, such as "lower abdominal pain" and "abdominal pain," are assumed by the system, but related terms at the same level of specificity, such as "left lower quadrant pain," are not assumed.

A typical user interaction with DXplain is illustrated in Fig 1. Examples of how the system helps the user select the appropriate terms during input are illustrated in Fig 2.

A second important factor relating to ease of use is the rapidity with which the user can enter the clinical manifestations and extract the desired information and interpretation. The system is designed to be largely self-explanatory. There is no need to read manuals: the beginning user can take advantage of menu selection; the experienced user can make use of an abbreviated command language to speed the interaction. The requirement for rapid time response was a critical design factor that influenced decisions made about the organization of the knowledge base in the computer. It requires about two minutes to complete the dial-in sequence to log on to AMA/NET and to connect to the computer located at Massachusetts General Hospital. The entry of the seven terms illustrated in Fig 1 required about one minute. Evaluation of the clinical data by the computer program and presentation of the interpretation and list of diagnostic hypotheses takes from 10 to 20 s.

Accurate and Comprehensive Medical Content

The development of a comprehensive knowledge base in medicine, whether printed or computer based, is a large effort. The merit of any decision-support system depends to a significant extent on the quality of the knowledge base used in formulating its recommendations. One aspect of any knowledge base, whether printed or computer based, is the inability of the author to certify that the entire knowledge base is totally accurate and comprehensive.

There are no methods to extract automatically the relevant information from the published literature. In fact, the published literature is not as useful as desired since it often does not provide the quantitative relationships between clinical manifestations and diseases that are required for a decision-support system. For example, one frequently finds statements like "symptom X is 'occasionally found' in the disease" or "it is 'not uncommon' to have symptom Y" or "the 'great majority' of the patients with the disease will demonstrate symptom Z."

To provide the necessary knowledge base for DXplain, we begin with the computer-based version of Current Medical Information and Terminology (CMIT), which is published and supported by the American Medical Association. (Ref. 17) Current Medical Information and Terminology contains summaries of information concerning the etiology, signs and symptoms, laboratory findings, and disease course for more than 3000 distinct diseases, disorders, and conditions.

To transform this knowledge base into one suitable for a decision-support system, it was necessary to carry out a considerable

amount of manipulation and additional content acquisition. For the disease list for DXplain, we combined some diagnoses from CMIT to form more inclusive definitions, while others were subdivided into more specific forms of the disease (eg, separate stages of a disease, forms of the disease specific to certain demographic groups, and forms attributed to different etiologic agents). Additional diseases were added when deficiencies in CMIT were noted.

As the first step in specifying the controlled vocabulary of terms to represent the clinical features of each disease, terms were extracted from the text of CMIT, yielding a list of some 6000 words and phrases. An extensive review of this list was undertaken to lend coherence to the vocabulary. Synonyms were merged where appropriate and similar terms were linked together in a hierarchical manner to express their relationships (usually in terms of such qualifiers as severity, duration, or anatomic location). The outcome was a term directory consisting of 4000 descriptors. As disease descriptions were compiled, 700 additional concepts were added to the directory.

We used a three-step process to generate the disease-term relationships of the knowledge base. First, a list was compiled from the CMIT data base and from expert judgment of all the terms that had some role in either supporting or ruling out a particular disease. Next, medical texts were reviewed to determine the frequency of each clinical finding in the disease. Where necessary, in circumstances of recent discoveries or obscure conditions, literature searches were conducted to supplement standard references. Finally, an estimate of the potential for the presence or absence of each term to evoke or refute the diagnosis was made.

This content development was an iterative process that was done by the system developers in collaboration with 13 physicians representing several medical disciplines. Because of the number of individuals involved, extensive discussions were required to reach a consensus on content and assignment of appropriate weighting factors for the relationship of terms to diseases. Once guidelines were established, authors were trained in filling out work sheets for each disease. Each work sheet included all terms that had been previously assigned, a prescribed set of demographic terms (age, sex, and duration of symptoms), and a generous number of blank lines for adding new terms. After the work sheets were completed, one of us (J.J.C.) reviewed them to ensure consistency of content, terminology, and assignment of evoking potentials.

The result of this work is DXplain's knowledge base consisting of descriptions of approximately 2000 diseases, about 4700 terms (signs, symptoms, and more), and some 65 000 relationships among them. On average, each disease description contains relationships to 35 terms. Each relationship identifies the frequency of the manifestation among patients with the disease and the strength with which a manifestation evokes a diagnosis for consideration.

From a practical viewpoint, it is impossible to verify completely all the elements in a knowledge base that is the size and complexity of DXplain. We believe that there must be a continuing effort to detect and correct incomplete or inaccurate disease descriptions. In addition, the knowledge base can never be static, but must continue to evolve as new knowledge is gained and new evidence is identified about each disease.

One of the major advantages of having the knowledge base reside on a single central computer is that the knowledge base can be updated easily and as often as necessary. The addition of a new term, disease, or synonym, the modification of the descriptor-disease relationship, or the enhancement of the program can be done quickly. Because these changes are immediately available to all users, the system can be dynamically responsive to user suggestions concerning deficiencies and improvements.

Provide Correct and Accurate Interpretations

In designing a differential diagnosis decision-support system, we assumed that the most useful assistance that can be provided to the practicing physician is to suggest the reasonable diagnoses that should be considered, given any particular set of signs and symptoms. We believe that in many complex diagnostic problems (and many not so complex), a major reason for not making the correct diagnosis is the failure of the physician to generate a differential diagnosis list that is comprehensive enough to include the correct diagnosis, yet sufficiently focused to include only the

more likely diagnostic possibilities.

The goal in DXplain is to assist the physician in two phases of the process of differential diagnosis: (1) to remind the physician of diseases that should be considered as possible candidates to explain the patient's condition and (2) to provide information about specific diseases that might be eliminated from consideration. We explicitly reject the objective of determining the "correct" diagnosis. We reason that the clinician will always have a more complete picture of the patient than will be entered into the computer program and that a more realistic goal for a decision-support system is to bring to the user's attention the plausible explanations for a patient's signs and symptoms. The user may then consider which diseases are appropriate to the case by applying common sense, clinical experience, and full knowledge about the patient and, possibly, by further interacting with the program.

DXplain is not intended to aid the specialist working in his/her specialty area. Thus, the cardiologist dealing with a patient with a complex murmur is unlikely to find DXplain very helpful; but the cardiologist dealing with a patient with abdominal pain may obtain useful assistance. The most obvious way in which DXplain can help is in suggesting obscure or rare diseases that may be rarely seen by most physicians. DXplain also may be helpful by suggesting diseases that present in atypical ways.

DXplain uses a relatively straightforward algorithm to select its list of plausible diagnoses. This algorithm has been described in a previous publication. (Ref. 14) The DXplain selection rule takes advantage of conditional probabilities and a scoring system similar to a Bayesian computation. Models such as this have been frequently used in other diagnostic decision-support projects, the most influential being the ranking algorithm used in INTERNIST/QMR. (Ref. 7,14) Our development of DXplain was strongly influenced by the experiences and the limitations of the original efforts of Miller and colleagues with INTERNIST, and their later development of QMR.

The knowledge base for DXplain contains more than 65 000 relationships between diseases and patient descriptors (or clinical manifestations). The format for these relationships and the data structures are similar to the format and data structures used in the INTERNIST/QMR system (Ref. 7) except that in DXplain terms cannot only support a given diagnosis, but can also contradict other diagnoses. The relationships in DXplain are concerned with three different elements: (1) term importance, (2) term frequency, and (3) term-evoking power.

Term importance is used to express how significant the particular term is in indicating the presence of disease. A high term importance is given to findings that can be identified with high reliability or are rarely found in healthy persons and, therefore, should be explained by some disease within the differential diagnoses.

Term frequency is used to identify how often a particular term is expected to occur in a specific disease. The possible values for term frequency can be one of seven different states ranging from "always" to "never."

Term-evoking power is used to identify how strongly a particular term supports the possibility that a specific disease might be present. This term is related to the concept of predictive value positive (the predictive value of a positive test -- this is the probability of a disease being present given the presence of a certain finding). The possible values for term-evoking power can be one of eight different states ranging from "certainly supported" to "weakly supported" and from "weakly contradicted" to "strongly contradicted."

DXplain uses the numerical values of these different relationships to derive the list of the diagnoses that should be considered (Fig 1). DXplain selects diseases to be included on this list on the basis of how well the manifestations of a particular disease match the descriptors that have been entered by the user. The diseases are presented to the user in two lists: "common diseases" and "rare diseases"; in addition, a serious disease (one that may require relatively immediate action) is so indicated on the list by an asterisk.

The user can request DXplain to explain why any specific diagnosis was included (Fig 3). DXplain will present the clinical findings entered by the user that support the selection of that disease, the clinical findings that

would not be expected in that disease, and additional clinical findings that would be expected if that disease was present. In this way, DXplain assists the user in understanding the logic used by the program and facilitates pattern matching by the user in comparing DXplain's disease description with his/her knowledge about the patient. The intent is to present sufficient information so that the user can always use his/her own clinical judgment as to the appropriateness of DXplain's interpretation.

The user can ask DXplain to consider a specific diagnosis that was not included on the initial list (Fig 3). DXplain will then present the same analysis, as described in the previous paragraph, for the diagnosis under consideration and, furthermore, will include this diagnosis in any later interpretation after additional findings are entered.

The user can change DXplain into an interrogative mode wherein the system will question the user about the presence or absence of significant findings that have the potential for clarifying DXplain's current differential diagnoses (Fig 4). This mode is particularly useful in helping the user select the clinical manifestations that are important without forcing them to enter a large number of less relevant findings. At any time in this mode, the user can interrupt DXplain to ask "Why?" ie, to ask DXplain to justify why this particular clinical manifestation is important. DXplain will respond by displaying the name of the disease that is being considered at that point in the interaction and the reason the particular finding might be important in confirming the presence of that disease.

DXplain's ability to explain and justify are key elements of the system. It is critical that this system not be perceived as a magic black box that can somehow provide the "answer" to a complex diagnostic problem. We believe that physicians will not accept DXplain as a useful diagnostic assistant unless the clinical interpretations seem reasonable and unless the system can offer explanations that are understandable and persuasive. (Ref. 18)

Convenient to Access

Almost a decade ago, Shortliffe wrote: "A recurring observation as one reviews the literature of computer-based medical decision making is that essentially none of the systems has been effectively utilized outside of a research environment, even when its performance has been shown to be excellent." (Ref. 8) For the most part, this observation is still true today. One important barrier is that the practicing physician cannot easily access a computer-based decision-support system from his/her office, or any other location, at any time. There are a number of systems that are available in university hospitals and that are of great importance in the host institution and have considerable value as demonstration models. However, none of these systems provide support to the practicing physician on a national scale.

DXplain is unique in that the decision-support capability is easily accessible using only a simple computer terminal (a microcomputer can also be used to make the connection), a telephone modem, and a telephone call (usually a local number in most of the major cities of the United States). DXplain is also available in a similar fashion in Canada and Japan. There is no start-up cost associated with purchase of the programs or of the knowledge base. Many physicians already have the necessary technology to access DXplain since the needs are the same as those used for on-line bibliographic search services.

DXplain was developed with the support of the American Medical Association and is designed to be distributed to the medical community through AMA/NET -- a nationwide computer communications network sponsored by the American Medical Association. Physicians and other professionals can access the system through the AMA/NET. Medical schools and teaching hospitals can access the system either through AMA/NET or through the Massachusetts General Hospital Continuing Education Network. In both cases, the cost of accessing DXplain is directly dependent on the length of time one is connected to the system.

A subscriber to AMA/NET can also access information data bases (EMPIRES clinical reference citations, Medical Procedure Coding and Nomenclature, the Associated Press Medical News Service, and more), public information services (Centers for Disease Control Information Service, National Library of Medicine/National Institutes of Health Information Services, Adverse Drug Reaction Reporting Form, and more), electronic

mail, and the Massachusetts General Hospital interactive medical education courses (Hoffer et al (Ref. 19)). AMA/NET also provides documentation and telephone support to its subscribers. (For information on AMA/NET, call 1-800-426-2873; for information on the Massachusetts General Hospital Continuing Education Network, call 617-726-3950.)

Evolve and Improve as a Result of User Criticism

A key element in the distribution of DXplain is an integrated electronic mail capability. At any point in the interaction a user may enter a comment or question into the computer system. This electronic mail is read at frequent intervals by the system developers at Massachusetts General Hospital and responded to as appropriate.

We view the plan for the continuing improvement and enhancement of DXplain as one of the more important aspects of its development. The major potential weakness of any diagnostic decision-support system such as DXplain is the quality and completeness of the underlying knowledge base. Evaluating a clinical decision-support system is difficult, both conceptually and in practice. (Ref. 1,11) Systematic clinical trials or formal outcome studies on the impact either of computer-based knowledge bases or of medical textbooks are logistically almost impossible. DXplain has been used by physicians for over 500 hours at more than 40 different test sites in the United States, Canada, and Japan. The initial user acceptance and peer review has been favorable, although the evaluation has been largely anecdotal.

The continuing refinement of DXplain will be most fruitful if the planned collaboration between the physician-users and the developers materializes. We expect and need the participation of physicians who will challenge the system with rare diseases and with uncommon manifestations of common diseases. The continuing critical review by DXplain users of the knowledge base and interpretations of the system will provide important feedback in the iterative process of knowledge base development.

SYSTEM LIMITATIONS

DXplain has a knowledge base that covers more diseases than are discussed in most textbooks of medicine, but in some areas DXplain is incomplete, eg, there is only limited coverage of dermatologic diseases, where diagnosis often depends on the visual appearance of the lesion. At present, there is only minimal coverage of diseases from psychiatry and orthopedics. DXplain presently allows the entry of only a limited set of laboratory test findings. The original design goal of DXplain was primarily focused on ambulatory medicine; as a result, the current version of DXplain does not allow the entry of many of the complex laboratory tests that are performed only in hospitals. We are continuing to add both diseases and terms, including the most common laboratory abnormalities.

DXplain can cope in only a limited fashion with the variations in the way that a disease can present based on its evolution over time, degree of severity, and the modifications introduced by therapy. In addition, DXplain does not identify complex disease patterns caused by the presence of two or more diseases in the same patient. DXplain considers each disease and its expected manifestations as unique entities. DXplain is unable to recognize how the manifestations of one disease can be modified by the presence of a second interacting disease. However, DXplain will attempt to select and present to the user all the individual diseases that might account for the more important findings so that the physician can use clinical judgment to carry out any appropriate recognition of disease patterns.

A number of authors have emphasized the importance of an explanation capability to encourage physicians to use decision-support systems. (Ref. 1,18) DXplain has an explanatory capability, but it is limited to the justification of why a particular disease should be considered (or ruled out), based solely on the likelihood of occurrence of the specific clinical manifestations in that disease. DXplain has no pathophysiological or anatomic knowledge and no ability to consider pathophysiological or anatomic reasoning.

The mere existence of data in a knowledge bank is, of itself, no guarantee of completeness and accuracy. The same professional judgment and critical appraisal are required when using DXplain as required when reading a medical textbook or discussing a patient case. In fact, since the computer program does not possess the depth of medical knowledge, the

wisdom of medical experience, or the ability of a colleague to reason, it would be wise to be even more critical of the computer's interpretation. One of the weaknesses that is common to every computer-based decision-support system is a lack of "common sense" and a relative inability to consider important personal, social, family, and employment factors of the particular patient. This deficiency is well illustrated by an anecdote in the conclusion of Shortliffe's article. (Ref. 1)

We believe it is critical that the physician retain the ultimate responsibility for identifying the correct diagnosis or diagnoses in any given patient. Using DXplain should be considered similar to consulting a medical textbook or journal article. DXplain should be used only as an adjunct, an information base, and a well-specified medical knowledge resource; DXplain cannot be a replacement for the clinician's knowledge and experience.

CONCLUSIONS

The potential contributions of computer-based decision-support systems are based on several factors: (1) the increasing complexity and scope of the medical knowledge base, (2) the increasing fragmentation and specialization of medical practice, (3) the increasing availability and affordability of powerful computer technology, and (4) the increasing willingness among physicians to utilize computer technology in all phases of patient care activity.

DXplain is an evolving computer system that uses an extensive knowledge base and relatively simple computational models to provide significant diagnostic problem-solving assistance to the practicing physician. The program allows the computer-naive user to enter a set of patient signs and symptoms and then generates a list of hypotheses that deserve consideration. The system also comments on the diagnostic relevance of each sign and symptom and suggests specific additional data elements that might clarify the differential diagnosis currently favored by the computer model. The advantages of a dynamic, interactive, evolving reference tool, such as DXplain, over static, passive textbooks and journal articles are exciting.

DXplain is unique in being a decision-support system that is easily and inexpensively available to a large number of physicians through nationwide medical information networks. A key element in the distribution of DXplain is the planned collaboration with its physician-users whose comments, criticisms, and suggestions will play an important role in modifying and enhancing the knowledge base and the algorithms used in the computer-generated interpretations.

The most important evaluation of DXplain will be made by the physicians themselves as they attempt to use the system in their daily practice. As DXplain is used in a variety of practices with a variety of information needs, we will learn whether this system is capable of providing clinicians with useful information in a timely manner. The measure of success is not whether the ultimate diagnosis is listed first or fourth in the DXplain list of plausible diagnoses, but whether the physician-users perceive that the use of the system has added to their understanding of the patient's problems. Through careful analysis of user interactions, comments, level of satisfaction, and system performance, we expect to learn much about DXplain's ability to provide assistance in making clinical decisions. Based on our experience during the testing phase, we are optimistic that DXplain will be a useful educational resource and an effective assistant to the physician in daily practice.

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Computer-based knowledge systems.
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ABSTRACT: In the first part of a two-part article, the author discussed the problem faced by physicians and other health care workers trying to keep up with the explosion of new medical information. In this, the second part, he discusses in detail the contribution that computers are making to the management and dissemination of medical information. Medical knowledge stored in computers may be used in four ways, but the author indicates that these four ways are interrelated and tend to overlap. One application of computer medical knowledge is hypertext. In this system, the reader is not limited to reviewing text and illustrations in a particular order, but can jump from tidbit to tidbit in any order which suits his need. A drawback of such systems is that the freedom of movement within a body of medical knowledge may result in the reader becoming lost or perhaps not appreciating the relationships between concepts which would be presented sequentially in a bound volume. A second, and very important, application of computer technology to medical knowledge is simply the maintenance of large knowledge files. Though such files might be called "databases", they are in fact knowledge bases and are more akin to reference books than to databases. A third contribution of computer technology to medical knowledge is specialized teaching aids. These systems are designed not for the professional seeking to add to his knowledge or perhaps look up a fact of which he is not certain, but rather for people to learn new things. The computer provides a presentation which may be individually tailored to the needs and abilities of the learner. The last category of computer applications to medical knowledge are the decision aids. These systems, somewhat akin to expert systems, help the physician by presenting the step-by-step sequences of decisions which must be made in the proper diagnosis of some symptoms or in the management of continuing treatment of patients. (Consumer Summary produced by Reliance Medical Information, Inc.)

TEXT:

In the first article I discussed medical knowledge and decision-making, the sources that doctors currently use to find this knowledge, and some of the drawbacks of these sources. I also described computer-based methods for searching bibliographic files. In this paper I concentrate on novel computer systems in which medical knowledge is not only stored and manipulated as text meaningful to human beings but is also encoded as symbols meaningful to computers.

There are four reasons to encode the knowledge held in a computer system:

- * To allow a computer user to move freely between passages of text, illustrations, or even sound recordings in a non-linear "hypertext" document.
- * To help a computer user find specific details in a large mass of medical facts stored in a "knowledge base", the electronic equivalent of a reference book.
- * To allow the computer to teach the user, by itself finding relevant details in its knowledge base that the user does not know (a teaching aid).
- * To allow the computer to help the user solve clinical problems, by itself finding details in the knowledge base that are relevant to the patient (a medical decision aid).

The key properties of hypertext, knowledge bases, and teaching and decision aids are listed in the table. These four kinds of system tend to overlap: in general, the more helpful a system is in decision-making about individual patients, the narrower its coverage of medicine (fig 1). For simplicity, I shall look at each kind in isolation.

Hypertext and hypermedia

When we use a textbook, we do not usually start at the beginning and read on to the end. Instead, we turn to figures or references on other pages, refer back to explanations in preceding chapters, and use glossaries and appendices to enhance our understanding. When text is stored on computer in the conventional way we are denied this instant access that the paper version gives us. However, these links can be recovered, and even enhanced, by the use of hypertext techniques [1] where links or short-cuts are provided between parts of the text. For example, a "definition" link may connect a word in the text with its glossary entry, while "see also" links draw attention to related sections of text. Frequently these links are shown as "buttons" or bold text on the computer screen, and users navigate through the system by selecting these items with a pointing device (mouse). Development of these systems can be difficult, especially if there is more than one author, since one has to keep track of multiple passages of text and their links as the work goes through successive revisions. Hypertext systems are now widely available outside medicine, guiding the uninitiated through software packages and tourists through airports. The Gosta's book project [2] is a medical hypertext system with 3000 links to help primary care physicians browse through the clinical and laboratory features of diseases.

Hypertext alone is no substitute for books in which diagrams or photographs are important. Thus, developers are now incorporating high-resolution computer graphics, sound, and video pictures to produce "hypermedia" systems. These are most widely used in teaching, and I shall discuss them in the section on teaching aids.

The similarity of one "page" to another in computer systems, the lack of a real beginning and end, and the fact that some hypertext systems offer ten or more links per page can lead to users getting "lost in hyperspace". To present a coherent overview and to avoid disorientation, some hypertext systems include a "guided tour" or maintain a list of all pages the user has viewed. Other systems provide an "overview" showing the structure of the whole document. [3]

Medical knowledge bases

Databases, the computer equivalent of card indexes, provide an efficient means for storing and retrieving large amounts of well structured data. If the store contains medical information such as drug dosages or **disease** incidences rather than patient data, the term "medical knowledge base" is preferred to database. There is a risk of overlap in terminology here, since **disease** incidences are calculated from a patient database, but few systems hold both kinds of information. Most knowledge bases include a search program to enable clinicians with modest computer experience to identify valid search items from lists and to combine them logically to identify relevant material. Medical knowledge bases can be stored on a central computer, with remote access by telephone or network links, or can be duplicated on floppy disk or compact disk read-only memory (CD-ROM) and installed on personal computers.

[TABULAR DATA OMITTED]

The difficulties of establishing and maintaining medical knowledge bases are identical to those associated with paper-based knowledge collections, discussed earlier. They include the difficulty of ensuring that the details contained are current and correct, that the coverage is adequate for clinical use, and that the index uses clinically relevant terms. However, two problems that are specific to electronic media are the use of symbols rather than a subtle natural language and the need to express knowledge in a form that can be read by any program running on any computer.

The London Dysmorphology Database is an example of a medical knowledge base distributed on floppy disk. [4] This details the mode of inheritance and clinical signs of 2000 congenital malformation syndromes. An editorial panel regularly reviews 1000 journals and issues annual updates. If congenital malformation interest you, it is difficult to see how this system can be bettered.

Floppy disks are not the ideal vehicle for knowledge bases because they are fragile and have limited capacity. A reasonable limit is 6, which will contain roughly 9 million characters equivalent to 1500 text pages. Instead, CD-ROMs are now widely used. These contain up to 660 million characters (the equivalent of 30 complete copies of the Oxford Textbook of Medicine), cannot be altered, and are physically more robust than floppy

disks. One of the knowledge bases available on CD-ROM (medical librarians usually keep a catalogue) is OncoDisk: this includes an oncology textbook, the Physicians' Data Query, and a catalogue of cancer therapy protocols known to the US National Cancer Institute, with details of patient selection, monitoring, and treatment, and even the names of physicians using the protocol. Some physicians already carry a selection of such knowledge bases with a portable CD-ROM reader and a notebook computer, to help them answer questions about patient management.

To keep a knowledge base current, updates must be sent out--a major enterprise if more than three or four a year are needed or the number of users is large. One solution is to allow access to a copy held and updated at a central point. An example is the Edinburgh Poisons Information System, which holds chemical and clinical data on thousands of poisons. [5] Access is gained through a Prestel terminal connected to a telephone line, and the system currently handles over 40 000 inquiries a year. Disadvantages of such dial-up knowledge bases are the need for special, sometimes arcane, search languages, and the slowness and cost of telephone links.

To allow wider access to centrally held knowledge bases, there are proposals by the European Community and others for "open systems interconnection". Establishment of an electronic "global village" will require standardisation of the codes used for clinical terms: but linkage of heterogeneous medical nomenclatures such as the ICD-10, SNOMED, and Read clinical coding systems, even through the "Unified Medical Language System", [6] has yet to be achieved. The physical linking of computer systems is easier, with fast cable, fibroptic, or cellular phone links (which allow portable computers to communicate with their base [7]).

Teaching aids

Teaching aids likewise include a medical knowledge base and programs to frame and execute searches. However, they are designed to enhance knowledge and understanding by presenting facts, explanations, and examples at the user's own level, thus superseding the old "teaching machines" that subjected all students to the same material. The knowledge base might consist of facts about a disease, or differential equations linking physiological variables, together with a search program. These are coupled with a program that elicits and records the facts a student does not know by asking suitable questions. The search program then assembles the unknown facts, together with suitable text, to display remedial material, before retesting the student. More elaborate systems provide a glossary of terms and offer static or video images and feedback through voice synthesisers; many use hypertext techniques.

A slightly different approach is to use high-fidelity patient simulations, as in the "Mac" series. [8] 'MacMan', for example, consists of linked mathematical models describing the circulatory, respiratory, and fluid-balance systems with programs that allow the student to change key parameters and assess their effects on the simulated person; the mathematics are hidden behind an attractive graphic presentation which helps students to link their knowledge of anatomy and physiology and to learn about dynamic relations between body systems. [9] Students seem to like these commercial teaching programs. [10]

One reason why the early teaching machines were badly received is that isolated or gratuitously offered facts are not well remembered: students learn best when they are confronted with a problem, [11] especially if they are emotionally involved in its solution. Some of the technologies outlined earlier make it easier to simulate cases in realistic fashion. For example, it is now possible to include short sections of video showing a "patient" in a hospital setting with authentic background noises punctuated by a nurse requesting advice, and then give the user guidance according to his or her responses to an on-screen question. One annoying aspect of these systems is that a typing error or the wrong vocabulary can be misconstrued as ignorance. Research is now focusing on more "intelligent" tutoring systems.

The big drawback of all these teaching systems is the vast amount of work needed to assemble even a brief lesson, since there must be enough material to allow for all possible responses to each question. If the medium is interactive video, this means dozens, sometimes hundreds, of video clips, all of which must be filmed in the same location with the same actors. Consortia of medical schools and others are forming to build such programs, but new dilemmas have arisen such as the need for standards to

allow interchange of material, and the question of who owns copyright.

Medical decision aids

A medical decision aid has a **knowledge base** and search program similar to that of a teaching system, but contains a program that builds a patient model rather than a student model. At its simplest, this program may ask the user to type in responses to questions about a patient such as age, height, weight, and lung function results, and then formulates a suitable search of its **knowledge base**. In this example, the **knowledge base** contains formulae to predict normal lung function test results and information about what abnormal results mean. [12] Instead of symbols representing medical details or strategy articulated by expert clinicians, the **knowledge base** of some systems contains a mathematical distillation of a series of cases with known outcomes, such as the prior probabilities of **diseases** and the conditional probabilities of certain findings in patients with those **diseases**. [13] The programs that build the patient model and search the **knowledge base** comprise a "reasoner", which reconciles the clinical features of a patient logically or mathematically with the knowledge in the system, to produce inferences. Such inferences might include a list of possible diagnoses with their probabilities, [14] potential adverse **drug** reactions, [15] or the therapy recommended by an oncology protocol. [13]

The first computerised medical decision aid was built in the late 1950s, [16] and thousands have been made since then. They are best classified by their clinical role. One type interprets patient data--sounding an alarm, reporting on an ECG, [17] or highlighting abnormal laboratory test results. [12] The second kind requests the user to enter patient data, and proposes a differential diagnosis [18] or management plan. Decision aids of this sort are the commonest today, but they resemble a Greek oracle in their reluctance to allow their knowledge to be used for other purposes. [19] The third type allows a more flexible interaction, with more sophisticated search and model-building programs, so that user and system can negotiate jointly for solutions. [20,21]

Most medical decision aids use one of three reasoning methods--Bayes' theorem, decision theory, or symbolic reasoning or "artificial intelligence" techniques. Bayes' theorem tells us how to use probabilities derived from a database of past cases with a known outcome to calculate the probability of the outcome in an individual case. [14] Decision theory is an extension to Bayes' theorem that lets us add weightings representing the value of each possible outcome to a decision tree, to calculate the "expected utility". [22] Symbolic reasoning methods include the use of "if . . . then" rules and other complex computer models [23] to link clinical findings with their causes and management. All these reasoning methods have been refined since their introduction and are now being combined--for example, in directed acyclic graphs, [24] one of which [25] is shown in fig. 2. Other reasoning methods include obscure computational models inspired by the structure of brain. [26] These "neural nets" rely on a process called machine-learning, and their evaluation is far from easy. [27]

The patient simulators used by students can also be helpful to clinicians. For example, a program that predicts blood glucose profile over 24 hours with a specific insulin regimen [28] may allow a doctor to explore alternative managements for a patient in a series of computerised experiments that hold no risk for the patient.

Few of the developers of medical decision aids see them as anything other than animated reference books, complementing rather than replacing human knowledge. Not so Weed with his "Problem-Knowledge Coupler". [29] A coupler is a computer program designed to provide clinicians with all the medical details they need to tackle a specific clinical problem, without committing medical facts to memory. Couplers are available for some 15 common conditions at present: if widely adopted, such systems might have a revolutionary impact on medical education, but would leave their authors in a position of unique responsibility.

Medical decision aids have already proved themselves clinically, with the Leeds Abdominal Pain System halving perforated-appendix rates in a multi-centre study, [30] Pozen's chest pain system leading to a reduction in inappropriate admissions to a coronary care unit, [31] and ONCOCIN (a symbolic reasoner for assisting in protocol-driven care) improving the completeness of data collection in cancer patients. [32] Systems are being

built to address a clinical need, [33] but may raise complex medicolegal questions for their users and those who supply them. [34] However, there are also more immediate dilemmas for users and developers.

Limited scope of decision aids

No medical decision aid contains as much knowledge as a medical textbooks, and the intellectual and practical challenges of building and maintaining large knowledge bases to support doctors remain daunting. Although it is possible to express lower-level medical details in knowledge bases, making higher-level knowledge explicit is a complex "knowledge engineering" task that requires understanding about how to acquire, represent, and reason with knowledge. [23] There are similar problems with building large databases of patient cases and extracting summary measures from them to reason about new patients, who may not be drawn from a similar population. [35]

Some decision aids, however, have achieved good coverage of medicine. The INTERNIST system performed acceptably in diagnosis of a range of clinico-pathological cases from the New England Journal of Medicine. [18] It is now commercially available as 'QMR' on personal computers, covering over 600 diseases and 4300 patient findings. DXPlain is another broad-ranging system that was widely available through a computer network. [36] In Britain, the 'Oxford System of Medicine' is planned as a comprehensive flexible information system for general practitioners, and a prototype containing a fraction of the required knowledge has demonstrated that the project is technically feasible. [21] One alternative to building a single large **knowledge base** and then adding a reasoner is to integrate several different decision aids, perhaps even using different reasoning methods, into one flexible resource, such as the EXPLORER system built at Harvard. [3]

Difficulties of communicating with computers

Many people become frustrated when trying to persuade computers to do what is wanted. When a doctor feeds patient data into a decision aid, a good system will not only communicate its advice back but also convince the user that the advice is well based. With the 'QMR' system it took an experienced user between one and four hours to enter enough patient data to generate a useful differential diagnosis. [37]

Most decision aids communicate only by text. 'IntelliPath', however, includes a laser videodisk storing 5000 photomicrographs. [38] These are used to augment text definitions of histological features and to show which features best distinguish between possible diagnoses. Some 300 copies of the system, which is supported by the American Society of Clinical Pathology, have been distributed. Other methods that may assist in rapid and accurate data entry include graphic "user interfaces" (fig 3), handwriting and speech recognition, [39] and direct interviewing of the patient by computer. [14] The ideal, however, is to integrate decision aids with an electronic medical record, so that all relevant data are then available, as with the HELP system. [40]

How do decision aids explain their advice to the physician? One system allocates "weights of evidence" to each clinical finding; [14] others use their symbolic knowledge about anatomy, pathophysiology, or mechanisms of drug action to generate textual explanations of their reasoning; [23] yet others are able to explain not only how they arrived at their advice, but also how it would have differed had certain patient features been absent, or why an alternative explanation is implausible. However, as with intelligent tutoring systems, it is often difficult for the system to understand what kind of explanation is required.

Need for evaluation

A major concern is that computers, like doctors, are often unable to admit their ignorance. They also have enormous placebo power, exacerbated by the term "expert system", which may cause inexperienced doctors to accept their advice without question. Before any system is used to support patient care, we must be confident that it is giving sensible advice. The content of a decision aid's knowledge base, the rigour of its reasoning, and its performance on suitable test cases must all be examined. [41] Even if the decision aid's performance is promising, it may still lack beneficial impact if it is difficult to use or gives implausible advice: [42] as with drugs, controlled clinical trials are the only way to assess their impact on doctors and patients. [41]

An ideal knowledge system

What every doctor needs is a portable, accurate, and adaptable source of medical knowledge. At present, nothing of the kind exists; but it is not too soon to think about the features required of such a system. What follows is based partly on the surveys of doctors discussed in the first paper. [43-45]

The system must be comprehensive

The system should cover the majority of diseases, therapies, and investigations as well as basic medical sciences, and should integrate text, graphics, moving images, and sound.

Knowledge contained in the system must be current, accurate, and verifiable

The certainty of the details stored should be stated, together with their sources to allow easy verification. The system should maintain its own record of the age of its knowledge, and updates should be issued regularly; all information should be safeguarded against unauthorised modification. To avoid ambiguity and to ease maintenance, a consistent vocabulary should be used, possibly even a logical language. [21]

Knowledge in the system must be easily accessible, where doctors see patients

The system should be portable and unobtrusive--preferably fitting into a white-coat pocket--and also cheap, indestructible, and workable without special equipment. To assist in clinical decision making, it must be fast and easy to use. Instead of a typewriter keyboard which is bulky and slow, the system should incorporate hand-writing recognition (like the new generation of pen-input computers). [46] The indexing system should include abbreviations and synonyms used in clinical practice; cross references to MeSH would facilitate literature searches. To help users absorb new material, updates should include digestible text overviews, analogous to the reviews and editorials in the medical weeklies.

The system should be adaptable

Since clinicians will be using the system throughout their working day, it should accommodate electronic notes and be adaptable to their own preferred terms or abbreviations. This could be achieved if each doctor carried a personal electronic badge which broadcast their identity and other data to the system in their hands. [7] The system should also be able to adapt itself to specific clinical problems, tailoring its reports and advice according to patient features. To do this, it could be linked by cellular radio networks to clinical data systems. This would also help it to predict, from information on who was using it and where, what knowledge the physician might need next--"anticipatory computing". [47]

Conclusions

There are few systems that meet even one of the above criteria, but advances in information technology will make the ideal knowledge system technically feasible. Furthermore, developments in medicine itself, and in the administrative framework surrounding it, suggest that the intellectual and practical challenges will be met.

One development is that medical societies are taking increasing responsibility for their members' knowledge as well as their professional competence. [48] Thus, specialty societies are defining management protocols, minimum data sets, and the content of coding systems. However, establishing and maintaining a fund of medical knowledge is a major undertaking, and few specialty bodies will have the resources to do it.

Another development is the establishment of medical informatics as the discipline concerned specifically with the acquisition, storage, and communication of medical knowledge and data. [49,50] Training courses, academic departments, professional journals, and societies now exist, [51] together with a definitive textbook. [52] The big issues in medical informatics include how to represent and store medical knowledge electronically and how to help doctors extract knowledge from these stores and apply it to their patients. Collaboration with specialists in medical education, computer science, and medical cognitive science [53] will be necessary to resolve some of these questions. A further challenge is to find ways of evaluating and comparing the sources of knowledge, and of assessing their impact on medical decisions (and on patients).

If the medical profession could harness the medical, technical, and managerial skills and produce a system such as that described above, the quality of medical care could take a quantum leap forward. Some clinicians may argue that reliance on such support will degrade their skills. This was

the cry when Laennec introduced the stethoscope.

These two papers were written partly at the National Heart & Lung Institute, London, and partly while I held an MRC travelling fellowship at the Section on Medical Informatics, Stanford University. I gratefully acknowledge the assistance of colleagues at both sites, others who have contributed their time, and the staff of the Lister Hill National Center for Biomedical Communications, US National Library of Medicine.

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CAPTIONS: Characteristics of computer-based knowledge system. (table); The continuum of medical knowledge systems. (graph); The directed acyclic graph underlying the ALARM anesthesia monitoring system (chart); Sample screen from ONCOCIN system. (diagram)

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SPECIAL FEATURES: illustration; table; graph; chart; diagram

INDUSTRY CODES/NAMES: HLTH Healthcare

DESCRIPTORS: Medicine--Data processing; Computer-aided medical diagnosis
--Evaluation

FILE SEGMENT: HI File 149

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11/9/15 (Item 10 from file: 148)
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09355604 SUPPLIER NUMBER: 19212526 (THIS IS THE FULL TEXT)
UCSF Launches Website "HIV InSite," A Comprehensive Online Gateway to AIDS Knowledge.

Business Wire, p3170259

March 17, 1997

LANGUAGE: English RECORD TYPE: Fulltext

WORD COUNT: 1382 LINE COUNT: 00118

TEXT:

SAN FRANCISCO--(BW HealthWire)--March 17, 1997--UC San Francisco AIDS specialists announced today (March 17) that anyone with access to a computer and to the "world wide web" can now obtain the most comprehensive, credible and trustworthy HIV/AIDS information available online with just a click of the mouse.

The top-rated UCSF AIDS Program at San Francisco General Hospital and the UCSF Center for AIDS Prevention Studies (CAPS), programs of the UCSF AIDS Research Institute, have created "HIV InSite" -- a one-stop shop for reliable, peer-reviewed AIDS information and the only website in existence that contains research written, edited and maintained by frontline AIDS researchers from a health sciences institution.

The address for the site is <http://hivinsite.ucsf.edu>.

"Reliable, timely information is essential to developing effective responses to the HIV epidemic," said Paul Volberding, MD, UCSF professor of medicine and director of the UCSF AIDS Program at SFGH. "The internet offers the potential to arm decision makers throughout the world with accurate up-to-date information, fostering the development of sound policies, enhancing prevention program development, and providing people living with HIV with information about treatments that may extend their lives."

Unfortunately, AIDS information reported in the popular media is often incomplete or inaccurate, and those most in need of information may sometimes become overwhelmed or lost in cyberspace, according to Thomas Coates, PhD, director of CAPS and the UCSF AIDS Research Institute.

"Information found at HIV InSite is reviewed and presented by the top thinkers in the AIDS field," said Coates. "No other institution can offer such depth in this area."

"With the launch of HIV InSite, patients, physicians, researchers, policymakers, health service providers, community organizers and journalists can be ensured that they are accessing the most reliable and current online resource for AIDS knowledge," Coates added.

Surfers of internet and users of "HIV InSite" will benefit from the breadth of in-depth information on the site -- from treatment, clinical drug trials, epidemiology and basic research to social and policy issues, prevention programs, population subgroups, and ethics. A distinct advantage of HIV InSite is the ability of the user to "see the big picture" of the AIDS topic he or she is researching, thereby adding value to the search, said Nicole Mandel, project manager of the web site.

For example, a reporter in New Mexico who might be writing a story about HIV infection among teenage runaways may dialup the internet to find out prevalence statistics. Accessing HIV InSite, the reporter will not only find out HIV rates among this group, which can be broken down by regions or states, but will find facts on homelessness and AIDS, a research study on HIV prevention for high-risk youth, and lists of local and national advocacy groups working with young people.

Another scenario might include an outreach worker at a community-based organization in North Dakota who is working with prisoners for the first time. Visiting HIV InSite, he or she will find a list of prison-based HIV prevention projects, an evaluation of a post-incarceration followup programs at San Quentin, and a review of prison condom distribution programs.

"The comprehensive nature of HIV InSite adds value to the researchers' information search," Mandel said.

Pages or subcategories of HIV InSite include:

Medical

This area provides comprehensive, practical and state-of-the-art information to meet the needs of health care providers, clinical researchers, health care policymakers and those living with HIV disease . Highlights include a "trials search" -- a user-friendly database of all HIV clinical trials in the U.S. in which users may search by **medical condition , drug or treatment** name, or location to find locations of appropriate clinical trials. Another feature is the **AIDS Knowledge Base** -- considered by many researchers to be the "bible" of HIV disease -- a 1600-page online textbook that is edited by AIDS specialists from UCSF and SFGH. In addition, users may explore case studies, **treatment** guidelines, and clinical fact sheets.

Prevention

The goal of this section is to help service providers, researchers, educators and others build stronger programs and studies in the effort to prevent HIV infections. HIV InSite offers detailed resources to answer some of the most pressing needs in prevention, including pages on epidemiology, prevention basics, frequently asked questions and their answers, resources and links to basic information about HIV/AIDS and safer sex, and HIV prevention interventions that have been evaluated for effectiveness and have been published in scientific journals and government reports.

Social Issues

This section is a searchable, comprehensive index of HIV social and ethical issues, resources and analysis. The site contains policy resource materials, such as statements, guidelines, reports and analysis, and new developments on topics ranging from adolescents to workplace issues. The section catalogues and organizes policy information and resources from numerous sources, including federal, state and local legislatures and agencies, the courts, professional associations, health policy research organizations, AIDS community-based organizations and advocacy groups.

U.S. Map

A map of the United States includes state-by-state statistics of the epidemic, as well as links to AIDS agencies and resources available in individual states. The AIDS epidemic in the U.S. varies by metropolitan area and state, and accounts for a total of 7% of all cases of HIV infection in the world.

HIV InSite will expand this geographic guide to HIV to include other areas around the globe, but in the meantime has links to other HIV InSite pages or other websites that have international data. HIV-infected individuals will also be able to locate clinical drug trials in their geographic area by keying in their medical information either through the U.S. map or through the clinical section of HIV InSite.

Key Topics

This section includes comprehensive information on key HIV and AIDS topic areas. Users may look here for news, articles, opinion pieces, documents, abstracts, bibliographies, contacts and other information. Among topics included in the exhaustive list are: advances in treatment, African Americans, condoms, discrimination, health care workers, international, lesbians, Native American, needle exchange, Ryan White Care Act, schools, sex workers, tuberculosis, vaccines and women.

The UCSF AIDS Program at San Francisco General Hospital, founded in 1983, is one of the oldest and largest programs of its kind in the world. With an internationally-renowned faculty and extensive clinical and research activities, the AIDS program is on the frontline of advances in clinical care for people with HIV. The program received the number one ranking from U.S. News and World Report in 1996 for the sixth year in a row.

CAPS, established in 1986, is the largest consolidated research effort in the country focusing on the social and behavioral aspects of AIDS prevention and early intervention. Research activities are carried out locally, nationally and internationally.

CAPS also conducts ethical studies and policy analyses of AIDS-related issues, provides a program of technology transfer and exchange with community-based organizations, and trains U.S. and international scientists in AIDS prevention. CAPS is made possible through grant funding from the Office of AIDS and the National Institute of Mental Health.

HIV InSite is made possible by a grant from the Henry J. Kaiser Family Foundation, an independent health care philanthropy based in Menlo Park, California. The Foundation is not associated with Kaiser Permanente

or Kaiser Industries. The Foundation supports research in four main areas: health policy, reproductive health, HIV policy, and health and development in South Africa. The Foundation also maintains a special interest in health policy and innovation in its home state of California.

Support for HIV InSite was also provided in the form of unrestricted educational grants from Bristol-Myers Squibb Company, Merck and Co., and Sun Microsystems. -0-

Note To Editors: To receive a press kit about "HIV InSite" and/or to interview website authors and editors, media should call UCSF News Services at 415/476-2557.

CONTACT: UCSF News Service

Rebecca Higbee, 415/476-2557

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DESCRIPTORS: California, University of (San Francisco)--Services; Online services--Services

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